A randomised controlled clinical trial of protein supplementation on the nutritional status in patients receiving continuous ambulatory peritoneal dialysis (CAPD) in Frere Hospital, East London

by

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Declaration with regard to independent work

I, Brigitte Leclercq, identity number 8905271026181, and student number 2012022014 , do hereby declare that this research project submitted to the University of the Free State for the degree Magister scientiae: A randomized controlled clinical trial of protein supplementation on the nutritional status in patients receiving continuous ambulatory peritoneal dialysis (CAPD) in Frere Hospital, East London, is my own independent work, and has not been submitted before to any institution by myself or any other person in fulfilment of the requirements for the attainment of any qualification. I further cede copyright of this research in favour of the University of the Free State.

_____ _____30/1/2015_____

Signature of student Date

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Dedication

A special dedication to all the participants (and their families) that took part in the trial, without all of them, this could not have been possible.

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AMA	Arm muscle area
BMI	Body mass index
BP	Blood pressure
CAPD	Continuous ambulatory peritoneal dialysis
CRF	Chronic renal failure
CKD	Chronic kidney disease
CRP	C-reactive protein
CVD	Cardiovascular disease
ESRD	End stage renal disease
GFR	Glomerular filtration rate
HD	Hemodialysis
KDOQI	Kidney disease outcomes quality initiative
MUAC	Mid upper arm circumference
NKF	National Kidney Foundation
nPNA	Normalized protein nitrogen appearance
PEW	Protein energy wasting
PD	Peritoneal dialysis
RRT	Renal replacement therapy
SA	South Africa
SGA	Subjective global assessment
TSF	Tricep skin fold
NHLS	National Health Lab Service

Conference contribution

The following abstract was accepted for presentation as a poster at the International Congress of Nephrology 2015 in Cape Town, South Africa, in the form of a poster presentation:

Purpose of the trial: To determine the effect of protein supplementation on the nutritional status of participants receiving Continuous Ambulatory Peritoneal Dialysis (CAPD) at Frere Hospital, East London, South Africa (SA) by conducting a randomised controlled clinical trial. To date no trial has been done in a SA population receiving CAPD, to assess whether protein supplementation, by means of a protein powder, will improve the participants' overall nutritional status.

Method: The experimental and control groups consisted of 13 and 13 participants respectively. The intervention group received *Protifar* powder (a protein supplement) at 0.65g/kg actual body weight, for a period of three months. All data was captured into *Microsoft Excel 2007* and exported to using SAS statistical software for analysis. The change from baseline to follow-up was calculated, compared between the two groups, and described by means of 95% confidence intervals for median or percentage differences. Ethics approval was obtained from the parties involved. Informed consent was obtained in English, Afrikaans or Xhosa. *Protifar* powder was supplied by Frere Hospital and no financial aid was provided by the manufacturing company.

Results: Socio-demographic information, medical history, CAPD regimen, biochemical measures and nutritional status were not significantly different between the groups at baseline. Most (61.5% in the experimental and 63.6% in the control group) had a normal BMI; most (69.2% in the experimental and 54.6% in the control group) had a normal to above average muscle mass, based on AMA; and most (61.5% in the experimental and 83.3% in the control group) were well-nourished based on SGA nutrition assessment tool. Most (92.3% in the experimental and 91.7% in the control group) had below normal serum albumin levels (median of 29g/L in both groups), and raised serum phosphate, urea and creatinine. The participants' dietary intake was mostly inadequate in total energy, protein, fat and carbohydrate.

During the intervention, no statistical significant difference was noted for anthropometry, AMA and most biochemical measures. The experimental group tended to have lower intakes of total energy, total protein, animal protein, carbohydrate and fat. The compliance to protein powder was generally good over the three months: 88.9%, 82.4% and 90.5% respectively.

At post-intervention the experimental group tended to have gained weight, had higher AMA measurements and SGA nutrition assessment tool scores; and increased serum albumin than at baseline; this trend was not statistically significant. Few participants (18.2% in experimental and no participants in the control group) received adequate dialysis in terms of the Kt/V formula, while none of the participants received adequate dialysis when comparing the creatinine clearance.

Conclusion: Clinical benefits (improved anthropometry and biochemistry measurements, SGA nutrition assessment tool score), but not statistically significant benefits of the protein powder supplementation were seen in the experimental group on overall nutritional status. More studies of a larger size and longer time period should be performed in patients receiving CAPD in different areas of SA, so to determine and improve their overall nutritional status.

Chapter 1: Introduction and motivation of trial

1.1 Introduction

Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for more than three months, with implications for health; and thus encompasses a variety of heterogeneous disorders which cause progressive structural or functional deterioration of the kidney and leads to different clinical presentation related to cause, severity and the rate of progression (KDIGO, 2013). CKD is characterised by progressive accumulation of pathological abnormalities or markers of kidney damage (Schrier, 2009). In patients with end stage renal disease (ESRD), renal replacement therapy (RRT), or dialysis, becomes necessary when renal function deteriorates so much that the accumulated waste products interfere with normal body functions, and physiologic changes occur which can no longer be controlled through the diet or with medication (KDOQI, 2006; Schrier, 2009).

In South Africa (SA) dialysis is initiated in patients with a GFR of less than 15ml per minute per 1.73m^2; and if the patient has one or more signs or symptoms of uraemia, fluid overload, poorly controlled blood pressure or evidence of malnutrition (Moosa *et al*., 2006:Online). Over the past years SA has experienced a dramatic increase in patients with ESRD who require dialysis (Moosa *et al*., 2006:Online). Therefore the need for dialysis facilities, for increased awareness of renal failure, and for proper diagnosis of patients in private and state institutions, are also increasing (Moosa *et al.*, 2006:Online; Abu-Aisha & Elamin, 2010).

Two options of RRT are available for South African patients, namely hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD). The first option, HD, requires a dialyser, which extracts waste products from the blood via an external dialysis membrane, and therefore requires the patient to visit a dialysis centre (Wilkens, Juneja & Shanaman, 2012; Schrier, 2009). Patients usually dialyse three times per week for about four hours per session (Moosa *et al*., 2006:Online; Wilkens, Juneja & Shanaman, 2012; Schrier, 2009). HD is generally preferred, as it is associated with a lower incidence of infection and longer survival time (Schrier, 2009), but has a great impact on the daily lives of patients with regard to time and travelling costs.

The second option, CAPD, is defined as dialysis using the semi-permeable membrane of the peritoneum and has several advantages over HD (Wilkens, Juneja & Shanaman, 2012; Moosa *et al*., 2006:Online).

Patients usually need four exchanges per day, but as these can be done at home, CAPD allows greater flexibility in daily activities than HD (Schrier, 2009), allowing patients to continue working and saving rural patients trips the dialysis centre (Moosa et al., 2006:Online; Schrier, 2009). Furthermore, CAPD requires no vascular access and is also associated with fewer cardiovascular complications (Moosa *et al*., 2006:Online). The lower cost of maintaining CAPD compared to HD, has also been well documented in many international studies (Berger *et al.,* 2009; Klarenbach & Manns, 2009).

1.2 The effect of CAPD on nutritional status

Despite the many advantages of CAPD over HD (Moosa *et al*., 2006:Online), CAPD causes more protein loss through dialysis than HD, leading to hypoalbuminemia (Schrier, 2009). The prevalence of malnutrition and wasting is significant in patients receiving CAPD (Burkart, 2002; Naicker, 2003; Abdu *et al.,* 2011; Blake *et al.,* 2011). Malnutrition in patients receiving CAPD has been shown to increase with hypoalbuminemia (Kopple, 1994; Fouque *et al.*, 2007; Blake *et al.,* 2011). Both CAPD-associated malnutrition and hypoalbuminemia, are in turn associated with higher rates of morbidity and mortality (Fouque, 2007; Blake *et al.,* 2011)

Optimal dialysis practices and dietary intervention is essential, especially in malnourished patients, to reduce morbidity and mortality; and improve nutritional status (Fouque *et al.*, 2007; Blake *et al.,* 2011). The most critical issue is to ensure an adequate nutritional intake, particularly due to the higher protein requirement of patients receiving CAPD (Schrier, 2009).

1.3 Nutritional assessment in patients receiving CAPD

The internationally recognised Kidney Disease Outcomes Quality Initiative (KDOQI), provides evidence-based clinical practice guidelines for all stages of CRF and related complications (KDOQI, nd:Online). KDOQI recommends that the nutritional assessment of patients receiving dialysis, should be a multi-dimensional one, as the optimal protocol to diagnose and monitor the response to nutrition intervention has not yet been identified (KDOQI, 2000). The recommended parameters with nutritional relevance include: body weight assessment, body composition assessment, clinical assessment, psychosocial evaluation, biochemical assessment and dietary intake (KDOQI, 2000).

1.4 Nutritional challenges

1.4.1 Malnutrition and supplementation in malnourished patients

Protein energy wasting (PEW) is defined as the lack of sufficient energy or protein to meet the body's metabolic demands, as a result of either inadequate dietary intake of protein, intake of poor quality dietary protein, increased demands due to disease, or increased nutrient losses (The free dictionary, nd:Online). The prevalence of malnutrition and wasting is significant in patients receiving CAPD (Burkart, 2002; Naicker, 2003; Abdu *et al.,* 2011), as well as common in patients with CRF (Kooman *et el.,* 1992; KDOQI, 2000; Schreiber, 2001; Calvo *et el.,* 2002) and this is associated with higher rates of morbidity and mortality (Avram *et al.,* 1996; Canada-United States of America (CANUSA) Peritoneal Dialysis Study Group, 1996; KDOQI, 2000; Jansen *et al.,* 2001; Pifer *et el.,* 2002). Therefore dietary and non-dietary interventions are vitally important to improve patients' nutritional status (Kalantar-Zadeh *et al*., 2011). Several factors influence the supplementation methods in patients receiving CAPD (Kalantar-Zadeh *et al*., 2011).

A dietary supplement is defined as a product intended for ingestion, that contains a dietary ingredient intended to add further nutritional value to supplement the diet (Food and Drug Administration, nd: Online). A dietary ingredient may be one, or any combination, of vitamins, minerals, herbs or other botanicals, amino acids, dietary substances that increases the total dietary intake, added in the forms of concentrates, metabolites, constituents, or extracts (Food and Drug Administration, nd: Online).

International generalisations have been made on certain aspects regarding supplementation in patients receiving CAPD. Oral supplements can increase the total daily energy and protein intake of patients receiving CAPD (Boudville *et al.,* 2003) and can provide an additional 7-10 kCal/kg/day (29.4-42kJ) and 0.3-0.4g/kg per day of protein (Kalantar-Zadeh *et al*., 2011). Kantar-Zadeh *et al.* (2011) recommend that in-centre meals or oral supplements are an inexpensive and feasible method that may improve patients' quality of life as well as their survival It is suggested that oral supplements should be given to patients two to three times per day, one hour after main meals, in order to meet the recommended dietary energy and protein requirements (Kalantar-Zadeh *et al*., 2011). Many studies declared the limitation, however, that patients receiving CAPD were either noncompliant or intolerant to dietary supplements, thus reducing the statistical power of possible improved nutritional status and decreased PEW observed in participants (Shimomura *et al.,* 1993; Heaf *et al.* 1999; Eustace *et al*., 2000; Aguirre-Galindo *et al*., 2003; Teixidó-Planas *et al*, 2005; Kalantar-Zadeh *et al*., 2011).

Inadequate nutritional intake, as well as intolerance to oral supplements, may be caused by slow gastric emptying associated with the intraperitoneal administration of dialysis (Van Vlem *et al*., 2002). Other factors which may contribute to wasting, include anorexia (due to nausea, emesis, medication side effects, uremia, inflammation and under-dialysis); inflammation (due to comorbidities and related to dialysis procedures); metabolic acidosis; endocrine disorders; and psychosocial factors (depression, low physical activity, loneliness and poverty) (KDOQI, 2000). Some evidence suggests that orally supplemented essential amino acids may be reasonably beneficial to patients with significant hypoalbuminea, but more studies are needed to warrant any recommendation (Bossola *et al.,* 2005)

The most important approach when supplementing these patients, is addressing the most life threatening complication that the patient is experiencing (Kalantar-Zadeh *et al.,* 2004). This is demonstrated in an example where the patient will die of a short term consequence such as PEW, before dying of risk factors associated with obesity (Kalantar-Zadeh *et al.,* 2004). This is known as the *'time discrepancy'* hypothesis (Kalantar-Zadeh *et al.,* 2004). This hypothesis is also demonstrated in two randomized controlled trials where a cholesterol lowering diet in patients with hyperlipidemia had no effect on their survival (Fellström *et al*., 2009; Wanner *et al*., 2005). One study suggests that controlling serum phosphate levels through strict dietary protein restrictions may cause increased mortality (Shinaberger *et al*. 2008). This is seen especially in patients with a low serum albumin and decreased normalised protein catabolic rate (Shinaberger *et al*., 2008). This could explain the contradictory observations of increased survival of patients who did not abide to strict rules of not eating any food during dialysis therapy (Kalantar-Zadeh *et al.,* 2005).

1.4.2 Low serum albumin

The most frequently used measurement in a patient with CRF is serum albumin levels (Mitch & Ikizler, 2010). The serum albumin measurement is easily accessible, easy to perform and affordable (Mitch & Ikizler, 2010; Kalantar-Zadeh *et al*., 2011). Low serum albumin is the strongest measure of mortality in patients with CRF (Lacson *et al.,* 2009), even when comparing it to other risk factors associated with a higher mortality, such as hypertension, hypercholesterolemia, diabetes mellitus and obesity (Lacson *et al.,* 2009).

1.5 Problem statement and significance of performing the trial

Very little data is currently available on the population receiving CAPD in the South African setting (Katz *et al.,* 2001) Only three previous studies have assessed the nutritional status of South African patients with CRF, in Johannesburg and Durban (Naicker 2002; Abdu *et al.,* 2011, Isla *et al.,* 2014).

The KDOQI Guidelines were used as the golden standard as these are broadly accepted clinical practice guidelines in nephrology, which have made a positive difference in the quality of care for kidney patients worldwide (KDOQI, 2000). The three South African studies reported a significant correlation between the SGA nutrition assessment tool score and anthropometric measurements, such as BMI and TSF. Malnutrition was common among patients receiving CAPD in these centres which highlighted the need for ongoing nutritional assessment and support of patients receiving CAPD (Naicker 2002; Abdu *et al.,* 2011, Isla *et al.*, 2014). The authors concluded that their results support the recommendations of KDOQI, that a number of assessment tools are needed to assess the nutritional status in renal patients and that these patients need nutrition support (KDOQI, 2000). However, to date no trial has investigated the effect of protein supplementation of South African patients on CAPD.

As no study to date has invesitigated the nutritional status of patients receiving CAPD in the Eastern Cape, the current trial was designed to profile this population with regard to their socio-demography and nutritional status. Frere Hospital, a 900 bed tertiary hospital in East London, was chosen to conduct the trial at, as it is one of the biggest CAPD dialysis units in the Eastern Cape area. Frere serves the whole Amatola district and also draws patients from the Northern and Eastern parts of the Eastern Cape. Frere Hospital therefore serves patients receiving CAPD who reside in a large, rural area of the province.

Isla *et al* (2014) found that many South African patients on CAPD live far away from the dialysis centre, reflecting the main advantage of PD over HD. The current study aimed to investigate the distances participants have to travel to the PD clinic in the Eastern Cape. Furthermore, the trial included several nutritional parameters from previous South African studies, such as BMI, AMA, SGA nutrition assessment tool, and biochemical measurements (Naicker 2002; Abdu *et al.,* 2011).
What makes this study unique in the South African setting, is that the trial also investigated how protein supplementation of the diets of the study population, in the form of a protein powder, would impact on their nutritional status over a three month period.

The information from this trial could provide valuable scientific input in terms of the effect of a protein powder supplement on the various parameters of nutritional status (anthropometric measurements, SGA nutrition assessment tool, biochemical measures and dietary intake) in patients receiving CAPD. The information could also be used to inform clinical practice and to develop guidelines and protocols for the renal unit of Frere Hospital and the greater Eastern Cape region to ensure optimal patient treatment.

Factors that need to be taken into account includes the various socio economic factors patients are faced with and the distances they have to travel to the PD clinics, and to make facilities easier to use and easier to access. This supports the guidelines for the optimal care of patients receiving chronic dialysis in SA, as set out by the South African Renal Society in March 2006 (Moosa *et al.,* 2006:Online). Recommendations in the latter document state that the guidelines should be reviewed at least every two years (Moosa *et al.,* 2006:Online). The current trial could therefore aid the process of updating the latest South African guidelines, particularly in reference to the nutritional management of patients receiving CAPD. Furthermore, hospital stay due to malnutrition and complications of patients recieving CAPD (such as fluid overload, hyperkalemia, hyperphosphatemia) amount to a huge financial burden on the already fragile health care budget in SA. A potential benefit of this study to the broader health care system could involve the lowering in health care costs due to effectively identifying, reacting and treating complications in patients receiving CAPD.

1.6 Aim and objectives

1.6.1 Aim

The aim of this trial was to describe the socio-demographic characterisitics and nutritional status of participants receiving CAPD at Frere Hospital, East London, as well as to conduct a randomised controlled clinical trial to determine the effect of protein supplementation on their nutritional status.

1.6.2 Objectives

In order to achieve the aim, the following objectives were determined:

1.6.2.1 Baseline assessment

The following information was recorded to determine the baseline nutritional status and provide randomisation criteria for the randomised controlled clinical trial:

- Socio-demographic information: age, race, gender, area of residence, number of people living with participant, employment status (Appendix 1);
- Medical history: aetiology of CRF, existing co-morbidities, medication (Appendix 1);
- CAPD regimen: duration, solution type, number of daily exchanges (Appendix 1);

- Nutritional status of participants receiving CAPD, including:
    - anthropometry measurements: edema-free body weight and height status, BMI, MUAC, TSF, AMA (Appendix 2);
    - SGA nutrition assessment tool (Appendix 3);
    - biochemical measures: S-albumin, S-sodium, S-potassium, S-phosphate, S-creatinine, S-urea, S-cholesterol (Appendix 4); and
    - dietary intake: 24-Hour Recall: energy, protein intake (total and high biological value) carbohydrate and fat intakes (Appendix 5).

1.6.2.2 Intervention

The study population was randomly divided into two groups according to the randomisation criteria (age, gender, serum albumin and duration on dialysis).

- The experimental group received a protein supplement in a powder form (intervention).
- The control group received the standard care of treatment which currently includes no protein powder (control).

The following were measured repeated monthly and data was recorded into the relevant appendices:

- anthropometry measurements: edema-free body weight, BMI, MUAC, TSF, AMA (Appendix 2);
- biochemical measures: S-albumin, S-sodium, S-potassium, S-phosphate, S-creatinine, S-urea (Appendix 4);
- dietary intake: 24-Hour Recall: energy, protein intake (total and high biological value) carbohydrate and fat intakes (Appendix 5); and
- record of protein supplementation: experimental group only (Appendix 6 – 8).

1.6.2.3 Post-intervention assessment (repeat of baseline)

The baseline assessment was repeated to compare the following outcomes between the two groups with regards to the effect of protein powder intake on the:

- Nutritional status of participants:
    - anthropometry measurements: BMI, MUAC, TSF, AMA (Appendix 2);
    - SGA nutrition assessment tool (Appendix 3);
    - biochemical measures: S-albumin, S-sodium, S-potassium, S-phosphate, S-creatinine, S-urea, S-cholesterol (Appendix 4);
    - record of protein supplementation: group one only (Appendix 6 – 8); and
    - efficiency of dialysis: transport status, weekly creatinine clearance, weekly K/tV (Appendix 9)

1.7 Outline of dissertation

The dissertation is outlined as follows

Chapter 1: Introduction and motivation of trial:

This chapter introduces the relevant background information on CAPD; motivation for the trial is discussed; and the aim and objectives are described.

Chapter 2: Literature review:

This chapter is a literature review which discusses the prevalence of CRF; the theory and practice of dialysis; the effect of the disease and treatment on the nutritional status of participants; tools to measure nutritional status; issues of malnutrition and supplementation in patients with CRF receiving dialysis; adequacy of dialysis; and the extent of the problem in SA.

Chapter 3: Methodology:

This chapter describes the methods used to conduct the trial. The study design; study population and sample selection; variables and operational definitions; sampling and study procedure; and techniques to ensure validity and reliability are discussed. The pilot study and the statistical analysis of the results are described. Ethical aspects are also described.

Chapter 4: Results:

This chapter describes the results of the trial.

Chapter 5: Discussion:

In this chapter the results of the trial are interpreted and discussed in the context of the current evidence on CAPD and supplementation of malnourished patients with CRF.

Chapter 6: Conclusions and recommendations:

The conclusions from the trial are set out in this chapter. Recommendations for policy, for practice, for health care professionals and for future research are discussed.

Chapter 2: Literature Review

2.1 Introduction

In this chapter chronic kidney disease is reviewed with regard to normal kidney structure and function; and the etiology thereof; progression to end stage renal disease; the role of ethnicity; pathophysiology, signs and symptoms; treatment options (HD and PD); markers of nutrition status; dialysis adequacy and the extent of the problem in SA.

2.2 Normal kidney structure and function

The main function of the kidney is to maintain homeostatic balance of fluids, electrolytes and organic solutes (Wilkens, Juneja & Shanaman, 2012). The normal kidney can perform this function over a wide range of dietary fluctuations in sodium, water and various solutes by continuous filtration and secretion and resorption of blood (Wilkens, Juneja & Shanaman, 2012). The kidneys filter approximately 1600 litres of blood per day or 20% of the cardiac output (Wilkens, Juneja & Shanaman, 2012). Ultrafiltrate (180 litres of fluid) is produced dailyu, but concentrated to 1.5litres of urine through the resorption of certain components and secreting other components (Wilkens, Juneja & Shanaman, 2012).

Each kidney consists of approximatelyn one million nephrons (Wilkens, Juneja & Shanaman, 2012). The nephron consists of a glomurulus, which is connected to a series of functional tubules: the proximal convoluted tubule, loop of Henle, distal tubule and collecting duct (Wilkens, Juneja & Shanaman, 2012). Each nephron functions independently, however when one segment of a nephron is destroyed, that complete nephron is no longer functional (Wilkens, Juneja & Shanaman, 2012).

The glomurulus is a spherical mass of capillaries, surrounded by the Bowman's capsule; and its function is to produce large amounts of ultafiltrate, which is similar to the composition of blood (Wilkens, Juneja & Shanaman, 2012). The production of ultrafiltrate is mainly passive, which is supplied by the renal artery and relies on the perfusion pressure generated by the heart (Wilkens, Juneja & Shanaman, 2012). Active transport aids the resorption of the vast majority of components that compose the ultrafiltrate and this requires a large expenditure of adenosine triphosphate (ATP) (Wilkens, Juneja & Shanaman, 2012).

The unique structure of the nephron, differences in permeability and the response to hormonal control, allow the tubule to produce urine which vary in concentration, volume, pH, osmolality, and sodium and potassiumconcentrations (Wilkens, Juneja & Shanaman, 2012). The urine produced is guided into the common collecting tubules and into the renal pelvis; which narrows into a single ureter per kidney, and each ureter carries urine into the bladder where it accumulates before elimination (Wilkens, Juneja & Shanaman, 2012).

The homeostatic mechanisms are interrelated, but some demands are placed on the kidney to regulate one substance at the expense of another substance e.g. sodium is the most important molecule in determining circulating volume and is regulated at the expense of other substances (Wilkens, Juneja & Shanaman, 2012). The kidney can excrete as little as 500ml or as much as 12 litres of urine when given a daily fixed solute load of 600 mOsm (the solute load representing the end waste products of normal metabolism) (Wilkens, Juneja & Shanaman, 2012). The majority of the solute load consists of nitrogenous waste, mostly end products of protein metabolism; such as urea, uric acid, creatinine and ammonia (Wilkens, Juneja & Shanaman, 2012). Renal function refers to the ability of the kidneys to eliminate nitrogenous waste products and azotemia is a condition when the normal waste products are not eliminated and accumulates in the blood (Wilkens, Juneja & Shanaman, 2012).

The control of water excretion is regulated by vasopressin (previously known as anti-diuretic hormone), a small peptide hormone excreted by the posterior pituitary (Wilkens, Juneja & Shanaman, 2012). A small rise in osmolality leads to vasopressin secretion and water retention (Wilkens, Juneja & Shanaman, 2012).

Another important function of the kidneys is to control blood pressure, through the rennin-angiotension mechanism (Wilkens, Juneja & Shanaman, 2012). Decreased blood volume causes the juxtaglomerular apparatus (cells of the glomerulus) to react by secreting rennin; which then acts on angiotensinogen in the plasma to form angiotensin 1, which is converted to angiotensin 2, a powerful vasoconstrictor and stimulus of aldosterone secretion (Wilkens, Juneja & Shanaman, 2012). Blood pressure will then return to normal as sodium and fluid are resorbed (Wilkens, Juneja & Shanaman, 2012).

The kidney is responsible for producing erythropoietin (EPO), which is a hormone for erythroid activity, in the bone marrow (Wilkens, Juneja & Shanaman, 2012). An EPO deficiency is a factor in severe anaemia, which is present in CKD (Wilkens, Juneja & Shanaman, 2012).

The kidney is also responsible for the production of the active form of vitamin D-1,25-$(OH)_2D_3$ and eliminating calcium and phosphorous (Wilkens, Juneja & Shanaman, 2012). Maintenance of calcium-phosphorous homeostasis involves complex interactions of parathyroid hormone (PTH), calcitonin and active vitamin D; with the kidney, bone and gut (Wilkens, Juneja & Shanaman, 2012). Active vitamin D promotes absorption of calcium by the gut and is responsible in bone remodelling and maintenance, as well as suppressing PTH production which is responsible for mobilization of calcium from bone (Wilkens, Juneja & Shanaman, 2012).

2.3 Definition of chronic kidney disease (CKD)

CKDis defined as abnormalities of kidney structure or function, present for more than three months, with implications for health. CKD thus encompasses a variety of heterogeneous disorders which cause progressive structural or functional deterioration of the kidney and leads to different clinical presentation related to cause, severity and the rate of progression (KDIGO, 2013).

The kidney undergoes a series of adaptions in a response to a decreased GFR to prevent ESRD (Wilkens, Juneja & Shanaman, 2012). There is an improved filtration rate in the short term, although it leads to an accelerated loss of nephrons and progressive renal insufficiency in the long term (Wilkens, Juneja & Shanaman, 2012). ESRD can result from a wide variety of different diseases with 90% of patients with ESRD having Diabetes mellitus, hypertension or glomerulonephritis (Wilkens, Juneja & Shanaman, 2012).

2.4 Classification of CKD

Kidney damage starts with changes that occur in the nephron (Schrier, 2009). In the long term, losses of nephron units occur, and any factor that increase glomerular pressure (for example hypertension) will accelerate this process (Wilkens, Juneja & Shanaman, 2012) as damage to glomeruli (through high blood pressure) leads to the progressive decline in GFR. The remaining glomeruli enlarge to compensate and preserve GFR (Wilkens, Juneja & Shanaman, 2012). These kidney adaptations work in the short term to improve renal function, but increase glomerular pressure in the remaining glomeruli (Wilkens, Juneja & Shanaman, 2012).

The more nephrons lost, the more the haemodynamic burden to the remaining nephrons, which leads to progressive glomerulosclerosis and sets up a vicious cycle of further nephron loss (Ide & Akani, 2011).

The consequent protein leakage through the affected glomeruli, results in enhanced tubule protein reabsorption, which initiates progressive tubule atrophy and interstitial fibrosis (Ide & Akani, 2011).

A slow, but progressive decline in renal function ensues, and eventually leads to renal insufficiency and ESRD (Wilkens, Juneja & Shanaman, 2012). The most important factors advancing this final common pathway of progressive nephron loss are hypertension, proteinuria, and hyperlipidemia (Ide & Akani, 2011). Risk factors which have shown to contribute to the progression of CKD to ESRD are Black ethnicity, female gender, smoking and drug use (Schrier, 2009), while obesity and a high salt intake are also associated with a poor outcome in subjects with pre-existing renal disease (Ide & Akani, 2011).

Kidney function is reflected by GFR, which is a measure of the rate at which the kidneys filtrate. Normal GFR is about 130 ml/min for males and 120 ml/min for females (Wilkens, Juneja & Shanaman , 2012) As CKD causes a progressive decline in excretory function, GFR is used to classify CKD into stages (KDIGO, 2013; Schrier, 2009), which is useful when care and treatment plans for patients need to be decided (Schrier, 2009; Moosa *et al*., 2006). The National Kidney Foundation (NKF) classifies by CKD according to different levels of deterioration in GFR (Schrier, 2009; KDOQI, 2002; KDOQI, 2000), as summarised in Figure 2.1. Stage one CKD is defined by the presence of kidney damage at the time of GFR measurement, with a GFR still above 90mL per minute per 1.73m^2 (KDIGO, 2013). Stage two is defined by the presence of kidney damage in the presence of mildly decreased GFR (60 – 89 mL per minute per 1.73m^2) (KDIGO, 2013). Patients are classified with stage 3 with a GFR of less than 60 mL per minute per 1.73m^2, regardless of kidney damage (KDIGO, 2013). Patients should be referred to a nephrologist when the patient's GFR is below 60 mL per minute per 1.73m^2 (Moosa *et al*., 2006). Stage three was recently further divided into two sub-groups (KDIGO, 2013). Stage 3a is defined by a mildly to moderately decreased GFR (45 – 59 mL per minute per 1.73m^2) and stage 3b is defined by a moderately to severely decreased GFR (30 – 44 mL per minute per 1.73m^2) (KDIGO, 2013). Stage four is defined as a severe decrease in GFR (15 – 29 mL per minute per 1.73m^2), and the patient is prepared for renal replacement therapy (KDIGO, 2013; Schrier, 2009). The final stage of CRF, stage five, is diagnosed when the GFR has dropped to less than 15 mL per minute per 1.73m^2 (KDIGO, 2013).

Another marker for progressive nephron damage, is the level to which albumin is excreted in the urine or albuminuria (KDIGO, 2013). Microalbuminuria is an important marker of glomerular injury and is used as a sensitive test for the detection of preclinical kidney dysfunction in diabetic patients (Ide & Akani, 2011), as an important prognostic indicator in hypertension, and to monitor patients with renal scarring (Ide & Akani, 2011).

Decreased GFR and albuminuria were previously not considered as CKD complications as such, but, following many epidemiologic studies, since 2002, are now identified as specific risk factors associated with adverse health outcomes (KDIGO, 2013). KDIGO classifies albuminuria into three categories, namely mildly increased, moderately increased, and severely increased. The International Society of Nephrology compiled a tool (Figure 2.1), combining GFR and albuminuria categories, to classify the relative risk of patient regarding CKD, and to advise on the frequency of follow up measurements (KDIGO, 2013).

				Persistent albuminuria catergories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30mg/mmol
GFR categories (ml/min/1.73m²) Description and range	G1	Normal or high	>90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

	Low risk: follow-up measurements annually if CKD is present
	Moderately increased risk: Annual follow up measurements once per year
	High risk: Annual follow up measurements twice per year
	Very high risk: Annual follow up measurements three times per year

Figure 2.1: Risk and prognosis of CKD based on GFR and albuminurea: Guidelines by intensity of colouring (KDIGO, 2013).

These general parameters, however, are based on expert opinion and underlying comorbid conditions should be taken into account (KDIGO, 2013).

2.5 Etiology of CKD

CKD develops many due to susceptibility to kidney disease, and/or factors that initiate kidney damage (KDIGO, 2013; Levey, Stevens & Coresh, 2009); and although many diseases are associated with kidney damage, the actual damage develops by only a few pathways (Schrier, 2009).

Non-modifiable risk factors are ethnicity and increased age, whereas modifiable factors that contribute to the decline of GFR, and associated albuminuria, include hypercholesterolemia, obesity, smoking, dietary salt intake, oral contraceptives and hormone replacement therapy (Ide & Akani, 2011). These risk factors are discussed in more detail below.

2.5.1 Ethnicity and birth weight

Various reports have documented higher prevalence of elevated albumin excretion in specific ethnic groups (Ide & Akani, 2011). There is, for example, a noticeable two to three times higher risk for ESRD among African American, compared to white patients with diabetes (Schrier, 2009). This has been linked to poor health practices, uncontrolled blood pressure (BP), poorly controlled glucose, and lower socio economic status (Schrier, 2009; Estacio *et al.,* 2000). Recent studies also suggest that the racial and geographic disparities in ESRD, and the increasing incidence rates, may have a fetal origin, as indicated by an inverse association with birthweight (Ide & Akani, 2011). Hoy *et al* (1999) suggested that intrauterine malnutrition impairs nephrogenesis, while Brenner & Cher (1993) proposed a mechanism by which impaired kidney development *in utero* may explanain reduced renal function later in life. Microalbuminuria and height have an inverse association in low birth weight children, arguing that fact that utero or early childhood low birth weights influence urinary albumin excretion in later life (Ide & Akani, 2011).

2.5.2 Gender and age

The incidence of ESRD is higher among males than females (Schrier, 2009; Coresh *et al.,* 2007) and elevated albumin excretion is found more frequently in men than women, especially at older age (Ide & Akani, 2011). In the general population, GFR decreases from the age of 30 by about 78 0.8ml/min/year (Ide & Akani, 2011). Assuming that a 30-year-old patient has a normal GFR of about 120ml/min, GFR will be about 70ml/min at the age of 80. A renal biopsy from the 80-year-old patient will reveal some atrophic glomeruli with tubule atrophy, with other glomeruli showing signs of glomerulosclerosis and glomerular enlargement and hypertrophy (Ide & Akani, 2011).

2.5.3 Metabolic diseases

The leading causes of renal damage are hypertension and diabetes mellitus, followed by glomerulonephritis (Schrier, 2009; Coresh *et al.,* 2007; Estacio *et al.,* 2000). Higher levels of proteinuria increase the rate of kidney disease progression making it an additional aggravator of ESRD (Schrier, 2009).

Patients with Type 1 and 2 diabetes have glomerular hyperfilteration and a slightly elevated albumin excretion rate associated with widespread endothelial dysfunction in the glomerular (and other) vascular beds, which progressively contributes to renal failure (Ide & Akani, 2011).

Increased urinary albumin loss is also linked to hypertension. Hypertension is characterised by widespread endothelial dysfunction causing glomerular hyperfilteration leading to microalbuminuria (Ide & Akani, 2011).

Obesity enhances the risk for glomerular hyperfilteration and hyperperfusion, and elevated albumin excretion is often seen in obese non-diabetic patients (Ide & Akani, 2011). The risk for glomerular hyperfilteration is specifically associated with abdominal obesity (Ide & Akani, 2011).

The Gubbio study, showed that the risk for elevated albumin excretion increased two-fold for each 1.03 mmol/L increase in plasma cholesterol (Ide & Akani, 2011). More rapid decline in GFR over time was reported in hypertensive patients with increased cholesterol levels (Ide & Akani, 2011).

2.5.4 Smoking

Smoking is associated with an increased risk for hyperfiltration, impaired filtration and albuminuria (Ide & Akani, 2011). Renal function impairment and proteinuria is associated with life time exposure to tobacco, but not necessarily the current level of smoking (Ide & Akani, 2011). The progression of kidney damage, and thus proteinuria, is also more pronounced and progresses faster in patients with Type 1 and type 2 diabetes, as well as in patients with lupus nephritis and polycystic kidney disease, who smoke (Hallan & Orth, 2011; Schrier, 2009).

2.5.5 Sodium intake

Higher sodium intake is independently associated with a higher urinary albumin excretion (Ide & Akani, 2011) and also predicts mortality and the risk for coronary disease (Ide & Akani, 2011).

2.5.6 Drug use

Heavy and daily use of non-narcotic drugs, such as analgesics (aspirin, paracetamol, pyrozolones, phenacetin) and caffeine, codeine or barbiturates over many years increases the risk for CRF (Schrier, 2009).

The use of oral contraceptives and hormone replacement therapy is also associated with enhanced urinary albumin excretion (Ide & Akani, 2011).

Increased renal vascular resistance and filtration fractions have been reported in women who use oral contraceptives (Ide & Akani, 2011).

2.6 Pathophysiology, signs and symptoms of CKD

Advanced ESRD presents with many problems related to the kidney's inability to excrete waste products, leading to uremic syndrome, PEW, altered electrolyte and hormonal responses, acid-base disturbances and renal osteodystrophy (Wilkens, Juneja & Shanaman, 2012). Disorders associated with acid-base imbalance in CRF are described in Figure 2.2.

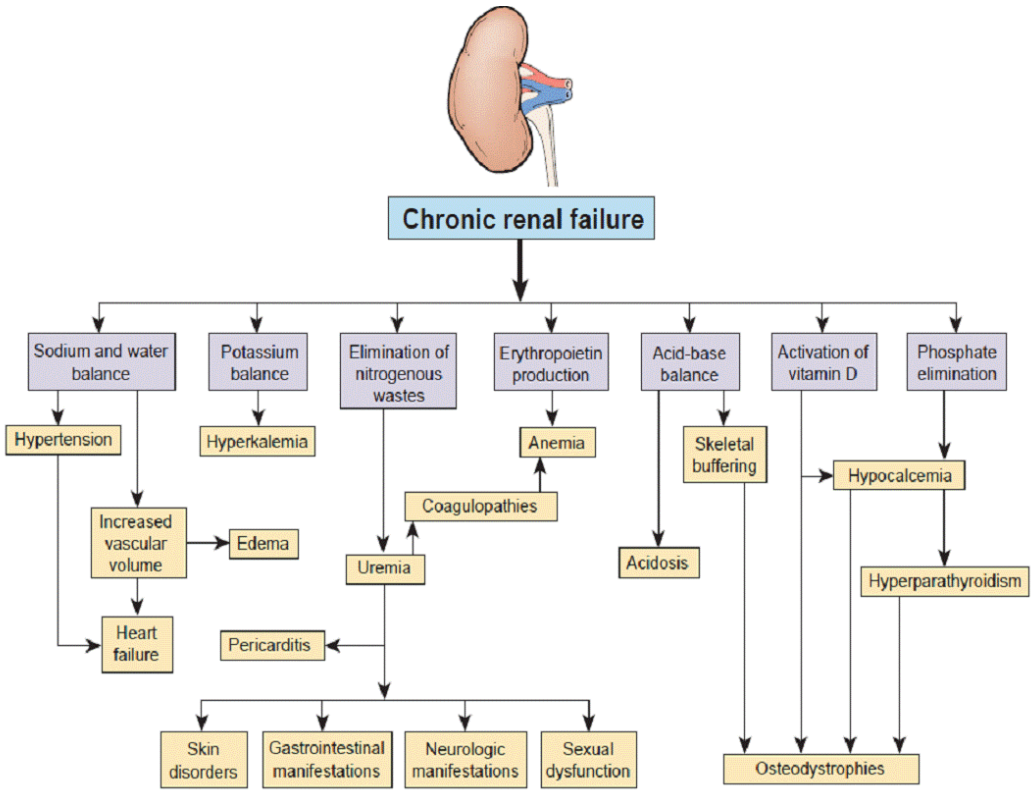

Figure 2.2: Manifestations of CRF: Disorders of the acid-case balance (nd: Online, Available at http://intranet.tdmu.edu.ua/data/kafedra/internal/i_nurse/classes_stud/RN-BSN%20Program/Full%20time%20study/Second%20year/methods%20of%20diseases%20diagnostics%20with%20the%20basis%20of%20clinical%20pathophysiology/27.%20Methods%20of%20investig%20during%20pathol%20of%20urinary%20org.htm)

One of the key characteristics of kidney failure with a GRF below 15mL/min, is the inability to exctrete protein waste products, causing these to accumulate in the blood. Uremia, a clinical syndrome characterised by weakness, nausea and vomiting, muscle cramps and itching, occurs when the blood urea nitrogen rises above 1.5 mmol/L and serum urea above 25 mmol/L, although no reliable laboratory parameter directly corresponds with the onset of the symptoms of uremia (Wilkens, Juneja & Shanaman, 2012). Uremia may lead to neurological impairment due to the high level of nitrogenous waste in the body (Wilkens, Juneja & Shanaman, 2012).

Uremia-induced alterations such as increased energy expenditure, persistent inflammation, acidosis and multiple endocrine disorders, lead to excess catabolism of muscle and fat, and contribute to PEW (Carrero *et al.*, 2013). PEW develops due to many nutritional and catabolic alterations which occurr in CKD, and is associated with morbidity and mortality (Carrero *et al.*, 2013). Mechanisms involved in these alterations is summarised in Figure 2.3 (Carrero *et al.*, 2013).

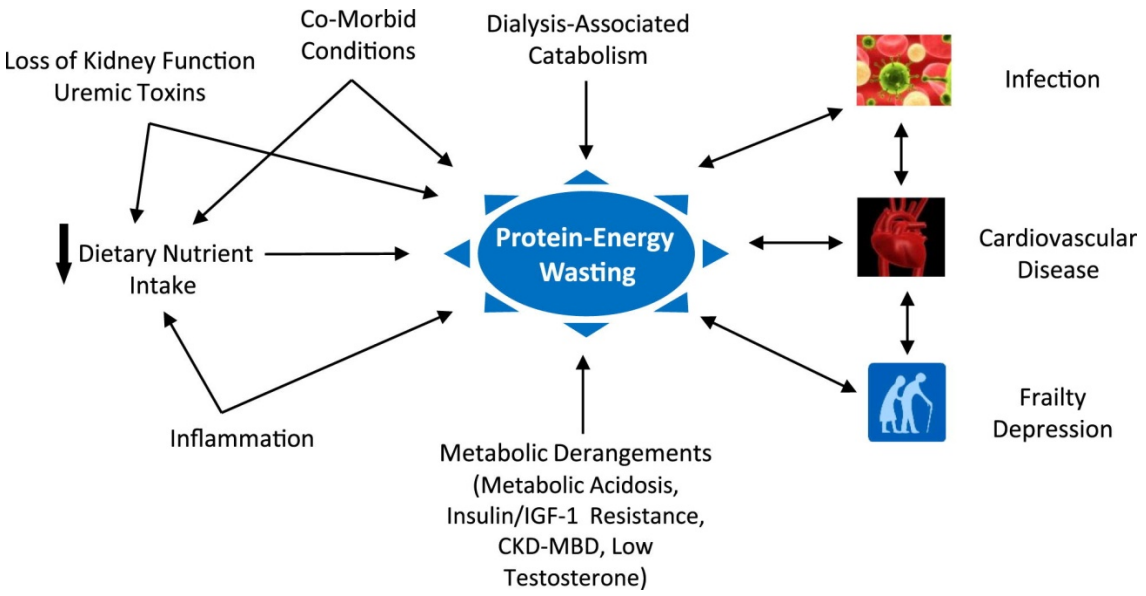

Figure 2.3: A conceptual model for the etiology of PEW in CKD and direct clinical implications (Carrero *et al.*, 2013).

Causes of PEW in patients with CKD include decreased protein and energy intake, hypermetabolism, metabolic acidosis, decreased physical activity, decreased anabolism, dialysis, co-morbidities and lifestyle factors (Carrero *et al.*, 2013). Anorexia due to a dysregulation of circulating appetite mediators, hypothalamic amino acid sensing and the excess nitrogen-based uremic toxins, contributes to a decreased protein and energy intake (Carrero *et al.*, 2013). Anorexia may also occur in these patients due to dietary restrictions, alterations in organs involved in nutrient intake, depression, and the inability to obtain or prepare food (Carrero *et al.*, 2013).

Hypermetabolism occurs in patients with ESRD due to an increased energy expenditure, which is accelerated by inflammation associated with increased circulating proinflammatory cytokines, insulin resistance secondary to obesity, as well as altered adiponectin and resistin metabolism. Hormonal disorders, such as insulin resistance and increased glucocorticoid activity also contribute to the hypermetabolism (Carrero *et al.*, 2013). Anabolism is decreased due to decreased nutrient intake, resistance to GH/IGF-1, testosterone deficiency and low thyroid hormone levels (Carrero *et al.*, 2013).

Dialysis also contribute to PEW due to nutrient losses into the dialysate, dialysis relatedinflammation and hypermetabolism, and loss of residual renal function (Carrero *et al.*, 2013). Co-morbidities including diabetes mellitus, coronary artery disease and peripheral vascular disease, congestive heart failure, and depression contribute to PEW (Carrero *et al.*, 2013).

Electrolyte imbalances may occur at GFR below 5 ml/minute, when hormonal adaptations are inadequate, and when water and electrolyte intakes are very restricted or excessive (Wilkens, Juneja & Shanaman, 2012). Electrolyte imbalances develop in the final stage of renal failure and trigger hormonal adaptations aimed at correcting these imbalances, but which cause their own complications (Wilkens, Juneja & Shanaman, 2012). Increases in serum potassium levels lead to increased aldosterone secretion to try and normalize serum potassium levels; but this also increases sodium retention, which in turn causes hypertension even in a patient who had normal blood pressure before (Wilkens, Juneja & Shanaman, 2012). Increases in the serum phosphate levels lead to increased secretion of parathyroid hormone (PTH) to try and normalize the serum phosphate, but this contributes to PTH-induced calcium resorption and bone loss, which may develop into renal osteodystrophy (Wilkens, Juneja & Shanaman, 2012). Increased concentration of potassium in extracellular fluid causes the cells in the kidney to release rennin, which in turn helps the kidneys to reabsorb sodium, leading to water retention and thus increases in the blood volume and increase blood pressure (Wilkens, Juneja & Shanaman, 2012). Renin activates angiotensinogen to angiotensin (Wilkens, Juneja & Shanaman, 2012). Angiotensin is responsible for vasoconstriction and thus narrows the diameter of the blood vessels, also increasing blood pressure (Wilkens, Juneja & Shanaman, 2012). Angiotensin, in addition, is responsible for the release of aldosterone from the adrenal glands, which signals kidneys to retain sodium and causes water retention, also contributing to an increase in blood pressure (Wilkens, Juneja & Shanaman, 2012).

In ESRF the kidneys are unable to produce erythropoietin (EPO) which is responsible for red blood cell production and this causes normocytic normochromic anemia (Wilkens, Juneja & Shanaman, 2012). Anemia increases the workload on the heart, which can lead to cardiovascular disease, which in turn further worsens CKD (Wilkens, Juneja & Shanaman, 2012). This usually stabilises with dialysis (Wilkens, Juneja & Shanaman, 2012).

Renal osteodystrophy may manifest as osteomalacia (bone demineralisation), osteitis fibrosa cystica (caused by hyperparathyroidism), metastatic calcification of joints and soft tissue (despite raised PTH and raised calcium, the serum phosphate elevated as GFR falls lower) and low turnover bone disease (unique to renal patients treated with vitamin D) (Wilkens, Juneja & Shanaman, 2012). In healthy patients, decreasing blood calcium signals the parathyroid glands to secrete PTH and the parathormone stimulates the activation of vitamin D (Wilkens, Juneja & Shanaman, 2012). Vitamin D and parathormone stimulate calcium reabsorption in the kidneys and vitamin D enhances calcium absorption in the intestines (Wilkens, Juneja & Shanaman, 2012). Vitamin D and parathormone stimulate osteoclast cells to break down bone, releasing calcium into the blood (Wilkens, Juneja & Shanaman, 2012). All these actions raise blood calcium levels, which inhibits PTH secretion (Wilkens, Juneja & Shanaman, 2012). In patients with renal failure, the activation of vitamin D is impaired, which lowers calcium levels and triggers PTH (Wilkens, Juneja & Shanaman, 2012). The kidneys then rely only on PTH, which increases calcium through bone resorption and also increases phosphate levels (Wilkens, Juneja & Shanaman, 2012).

2.7 Treatment options

CKD is associated with a broad spectrum of complications leading to adverse health outcomes (KDIGO, 2013). Figure 2.4 illustrates the progressive development of CKD, the likelihood of associated complications and the recommended treatment options (Levey & Coresh, 2012).

As discussed before, risks for development of CKD may be categorised either as susceptibility to renal disease due to socio-demographic and genetic factors, or exposure to factors that can initiate kidney disease (KDIGO, 2013). Abnormalities in renal structure are present before abnormalities in renal function (KDIGO, 2013). Earlier stages of renal failure are often asymptomatic and may be reversible; patients reaching ESRD usually need a transplant or RRT, and symptoms are experienced due to the complications of renal failure (KDIGO, 2013). RRT is usually needed in only 1% of patients with CKD, but at the cost associated with RRT, CKD is the most expensive chronic disease with 5% of annual budgets being consumed by 1% of the patient population (KDIGO, 2013). Therefore, early identification and treatment of patients with CKD holds economic and clinical benefits (KDIGO, 2013).

The prevalence of diabetes mellitus and hypertension, both risk factors for CKD, are growing at alarming rates in both developed and developing countries (KDIGO, 2013). Screening for these risks are vitally important for prevention, early diagnoses and treatment of CKD and co morbid conditions through interventions such as controlling blood sugar levels in a diabetic patient and limiting sodium intake to control hypertension (KDIGO, 2013). High risk groups such as patients with established diabetes mellitus, hypertension, CVD, and the elderly, also need to be regularly tested for CKD so that interventions can be introduced at an early stage (KDIGO, 2013). Targeting risk factors that are modifiable, may reduce both CVD in patients with CKD and prevent the progression of CKD to ESRD (KDIGO, 2013).

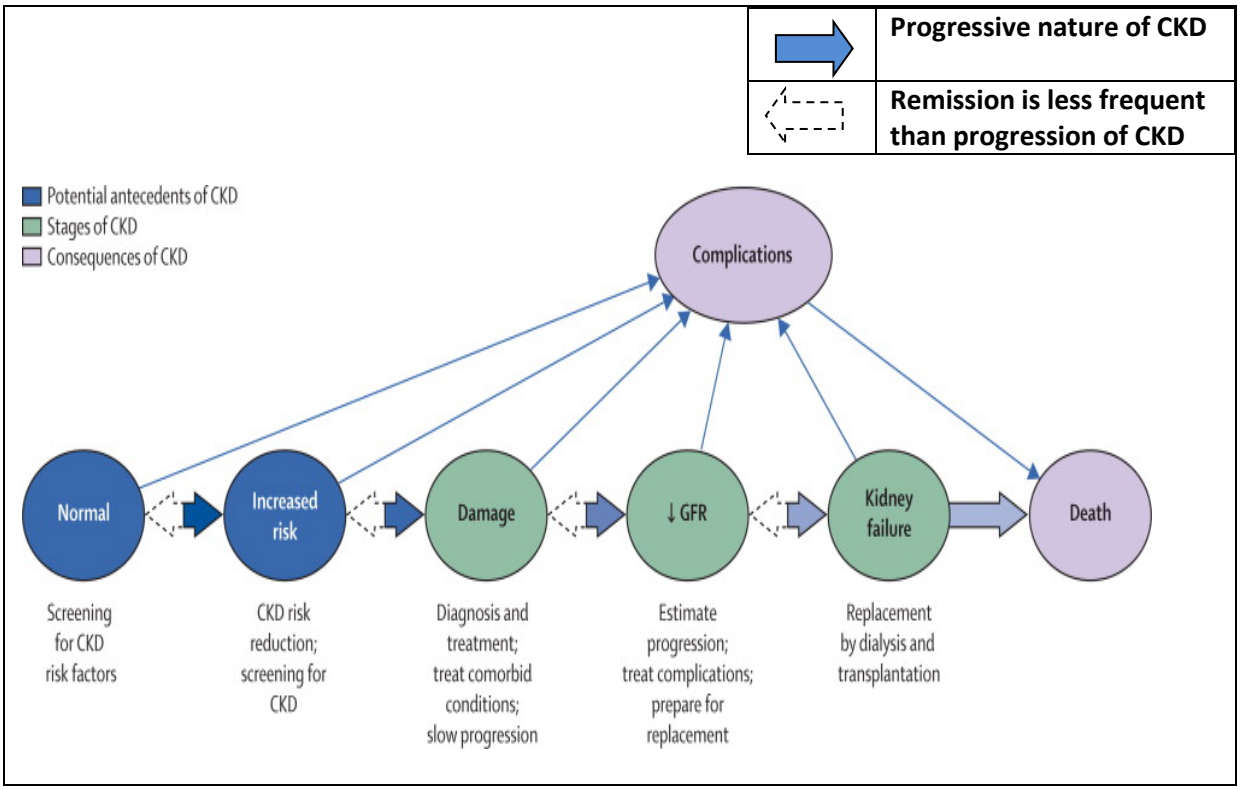

Figure 2.4: Conceptual model of CKD): Development, progression and complications of CKD and strategies to improve outcomes. (Levey & Coresh, 2012

RRT should be initiated when one or more of the following are present: symptoms or signs of renal failure (acid-base or electrolyte abnormalities, pruritus); inability to control volume status or blood pressure; progressive deterioration in nutritional status refractory to dietary intervention; or cognitive impairment (KDIGO, 2013). This often occurs when GFR ranges between 5 and 10 ml/min/1.73 m^2 (KDIGO, 2013).

Living donor renal transplantation in adults should be considered when the GFR is less than 20 ml/min/1.73 m^2, and there is evidence of progressive and irreversible CKD over the preceding 6–12 months (KDIGO, 2013). Conservative management should be an option in patients who choose not to receive RRT, and should be supported by a comprehensive management program (KDIGO, 2013). All stages of progressive CKD need to be managed in a multidisciplinary care setting; and include dietary counselling, education, transplant options, vascular access surgery, ethical care, psychological care and social care (KDIGO, 2013).

2.8 Dialysis to manage ESRD

RRT becomes an option in patients with ESRD (Schrier, 2009), when renal function deteriorates to the degree that the accumulated waste products interfere with normal body functions, and physiologic changes occur which can no longer be controlled through the diet or with medication (Schrier, 2009; KDOQI, 2006). Dialysis is initiated in South African patients at a GFR of less than 15ml/minute; and if the patient has one or more signs or symptoms of uremia, fluid overload refractory to diuretics, poorly controlled blood pressure, or evidence of malnutrition (Moosa *et al*., 2006). RRT needs to be carefully planned, as poor planning leads to an increased morbidity and mortality (Lacson *et al., 2009*; Moosa *et al*., 2006; KDOQI, 2006). Two options of RRT will be discussed, namely hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD).

Even in developed countries, such as in the United States of America, less than 15% of all patients with renal failure receive dialysis (Schrier, 2009; Coresh *et al.,* 2007). Jain *et al.*(2012) using renal registries followed by nephrology societies, health ministries, academic centres, national experts, and industry affiliates, calculated the prevalence of patients receiving HD and PD. According to most recent data approximately 1 550 000 patients across 130 countries were treated with HD; 38% received treatment in developing countries and 62% in developed countries (Jain *et al.*, 2012). In comparison, 195 555 patients across the 130 countries were treated with PD; 58% in developing countries (n=114 221) and 42% in developed countries (n=81 334) (Jain et al., 2012). Figures 2.5 and 2.6 respectively illustrate the number of PD patients in developing countries and developed countries in 2012 (Jain *et al.*, 2012). Worldwide the proportion of all dialysis patients treated with PD is 11% (Jain *et al.*, 2012). Only three percent of the dialysis population in Northern African countries are receiving PD (Abu-Aisha & Elamin, 2010).

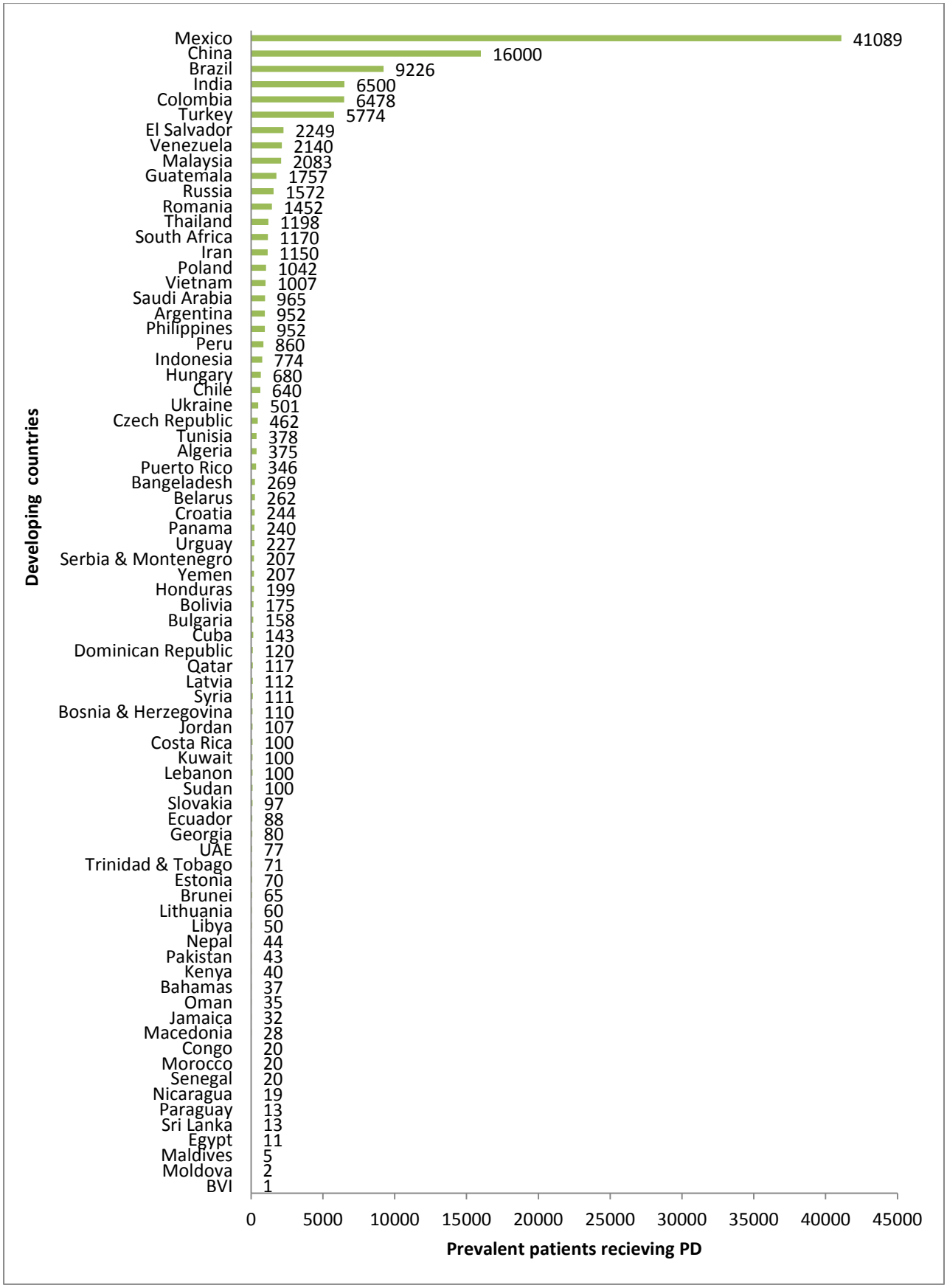

Figure 2.5: Prevalence of patients receiving PD in developing countries (adapted from Jain *et al.*, 2012)

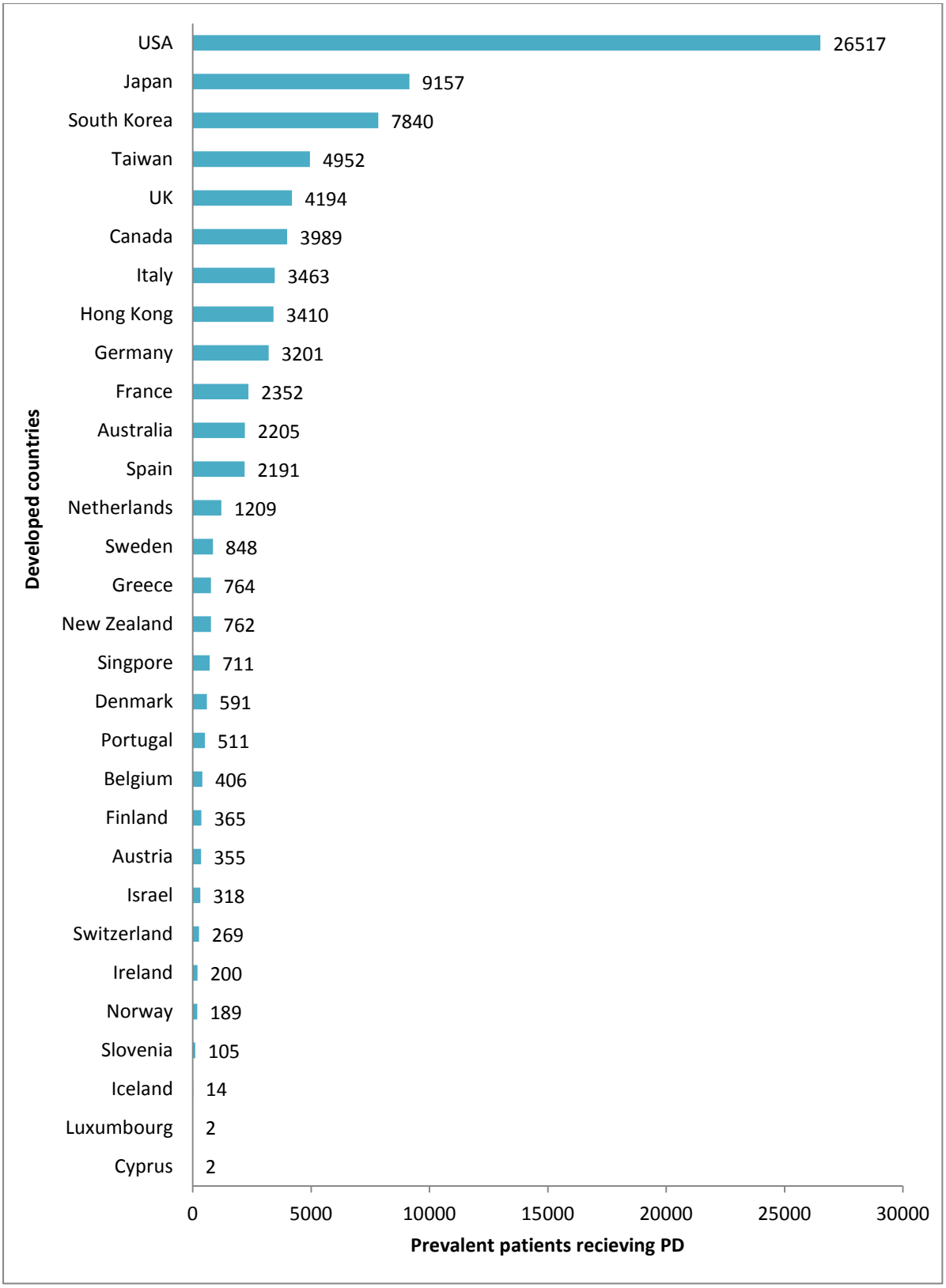

Figure 2.6: Prevalence of patients receiving PD in developed countries (adapted from Jain *et al.*, 2012)

2.8.1 Hemodialysis (HD)

HD requires the patient to visit a dialysis centre for each dialysis session (Schrier, 2009; Wilkens, Juneja & Shanaman, 2012). Patients usually dialyse three times per week for four hours per session (Schrier, 2009; Moosa *et al*., 2006; Wilkens, Juneja & Shanaman, 2012). Two options for permanent access of HD are available, as illustrated in Figure 2.7: either a native arterial venous fistula or an artificial arteriovenous graft (Schrier, 2009; Wilkens, Juneja & Shanaman, 2012). The first option is preferred due to a lower incidence of infection and longer survival time (Schrier, 2009). These access routes are surgically placed in the non-dominant arm, in the most distal position (Schrier, 2009; Wilkens, Juneja & Shanaman, 2012).

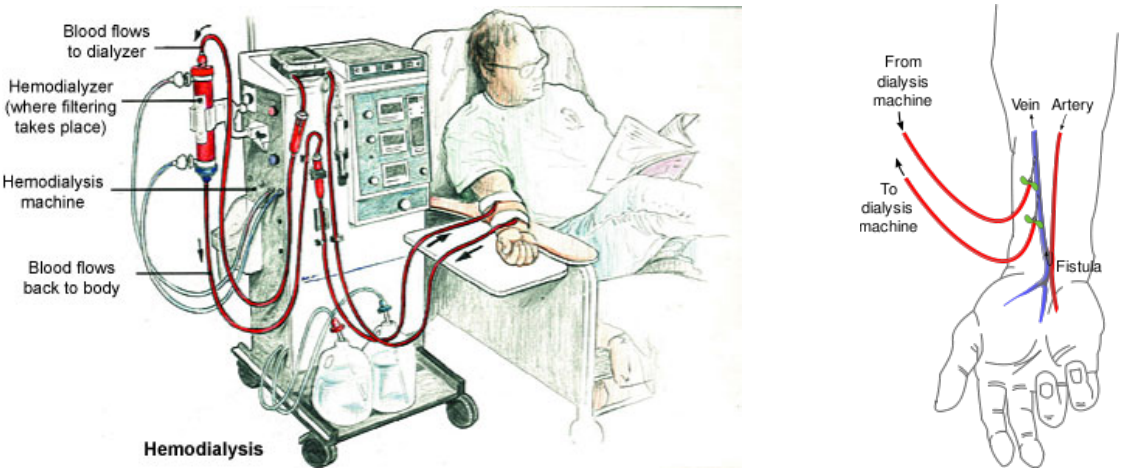

Figure 2.7: Hemodialysis (HD): Blood is circulated through a dialyser (artificial kidney) via tiny tubes made of a semipermeable substance where it is bathed by dialysate, a solution that selectively removes fluid and wastes (nd: Online, Available at http://www.thevirtualnephrologist.com/mobile/dialysis-g8.html).

The native arterial venous fistula may need up to six months to mature, and therefore careful planning needs to be done before initiating dialysis (Schrier, 2009; Wilkens, Juneja & Shanaman, 2012). The longer the fistula matures, the better the long term success (Schrier, 2009). The patient's vital signs are measured before and throughout the dialysis session. Two needles are placed in the fistula or graft and the blood is circulated through the artificial kidney or the dialysis machine (Schrier, 2009). Excess fluid and waste materials are removed by diffusion down the transmembrane pressure gradient and the concentration gradient, as well as using the process of osmosis and ultrafiltration (Schrier, 2009).

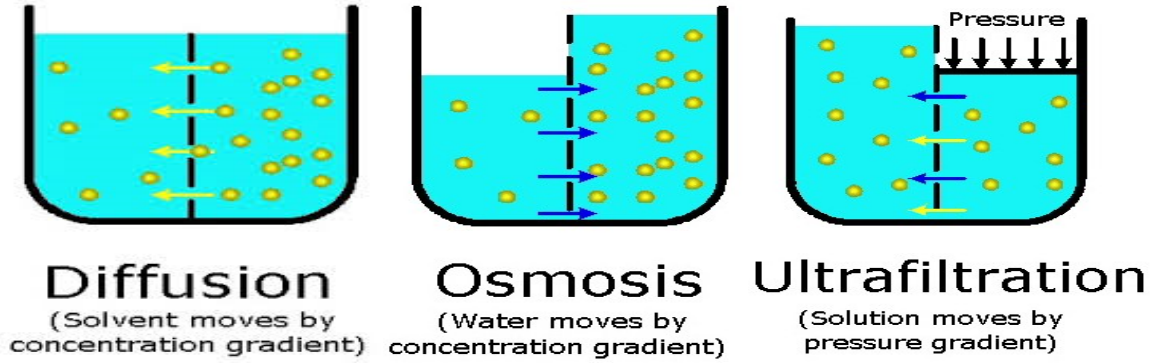

Figure 2.8: In the dialiser exchanges fluids and solutes across a semipermeable membrane using the principles of diffusion, osmosis and ultrafiltration (nd: Online, Available at http://www.toltec.biz/how_hemodialysis_works.htm)

Osmosis is defined as a passage of fluid through a semi-permeable membrane from an area of lesser concentration to an area of greater concentration in order to achieve equilibrium of solute. Ultrafiltration is defined as the process by which plasma water is removed from the blood related to an osmotic pressure gradient. The rate of ultrafiltration is highest in the beginning of an exchange when the osmotic gradient is highest (Advanced Renal Education Program, 2014: Online). The needles are removed at the end of the hemodialysis treatment session and local pressure applied to stop bleeding (Schrier, 2009).

2.8.2 Peritoneal dialysis (PD)

PD, is defined as dialysis using the semipermeable membrane of the peritoneum (Wilkens, Juneja & Shanaman, 2012). PD catheters are surgically inserted into the peritoneal cavity (Schrier, 2009). A waiting period of seven to ten days is preferred before using the catheter, to facilitate improved in-growth of the catheter in a sterile environment (Schrier, 2009). Dialysate containing a medium to high dextrose concentration is drained into the peritoneum via the implanted catheter with the assistance of gravity (Schrier, 2009) as illustrated in Figure 2.9. Blood is filtered by the peritoneum (the membrane that surrounds the abdominal cavity), removing the waste products. The period of time that the solution remains in the abdomen between exchanges, is called the dwell time. After several hours, the dialysate is drained, removing unneeded fluid and waste. Alternative dialysates with amino acids are also available for patients with diabetes mellitus, and will be discussed in more detail later in this chapter.

When resources are limited, patients must also be given alternative treatment options, such as conservative treatment, HD or a kidney transplant (Moosa *et al*., 2006). However, the lower cost of maintaining CAPD motivates it as the first choice for patients with CRF (Katz *et al.*, 2001).

The majority of patients in Africa on PD, live in SA (Abu-Aisha & Elamin, 2010). Thirty two percent of all dialysis patients in SA are treated with CAPD (Abu-Aisha & Elamin, 2010), as this is the only form of PD available in most South African institutions (Moosa *et al*., 2006). Patients usually need a minimum of four two-litre exchanges per day, which includes one overnight exchange (Moosa *et al*., 2006). The regime can be modified by changing the dwell time, volume (or exchange), or the number of dialysis exchanges per day (Moosa *et al*., 2006). The exchanges are performed manually at home by the patients, allowing greater flexibility in daily activities as they do not need to go to a dialysis centre, as required for HD patients (Schrier, 2009).

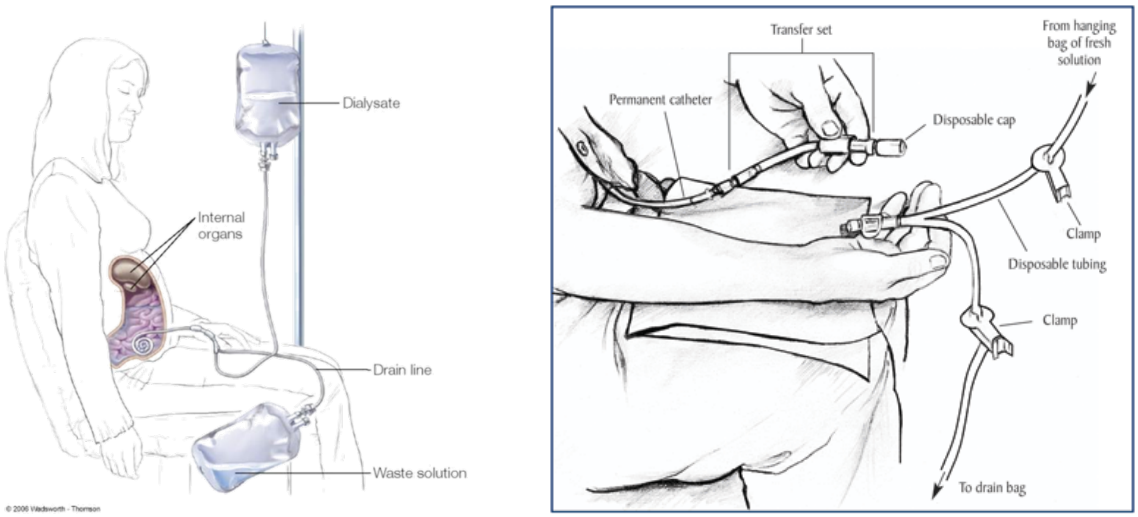

Figure 2.9: Continuous ambulatory peritoneal dialysis (CAPD) (nd: Online, Available at: http://kidney.niddk.nih.gov/kudiseases/pubs/peritoneal/images/Exchange.gif):

Automated PD is another peritoneal dialysis option, whereby a machine performs the overnight dialysis exchange (5 or 6 litre PD bag) instead of the patients manually doing the exchange. This gives the patient more flexibility during the day (Schrier R, 2009). In general, automated PD is superior to CAPD in optimising fluid and small solute removal in some patients, due to the automated technique that combines larger dwell volumes and long nocturnal sessions (Schrier R, 2009). A systematic review of three clinical trials, which included 139 patients receiving CAPD or automated PD, showed that CAPD and automated PD provide similar clinical outcomes regarding mortality, hospitalisation rates, risk of peritonitis and fluid leaks (Rabindranath *et al.*, 2007). The choice between CAPD and automated PD depend on the patient's lifestyle and medical prescription when economic factors do not play a role (Daugirdas, Blake & Ing, 2007). Figure 2.10 and 2.11 illustrates the CAPD versus APD use in developing countries and developed (Jain *et al.*, 2012).

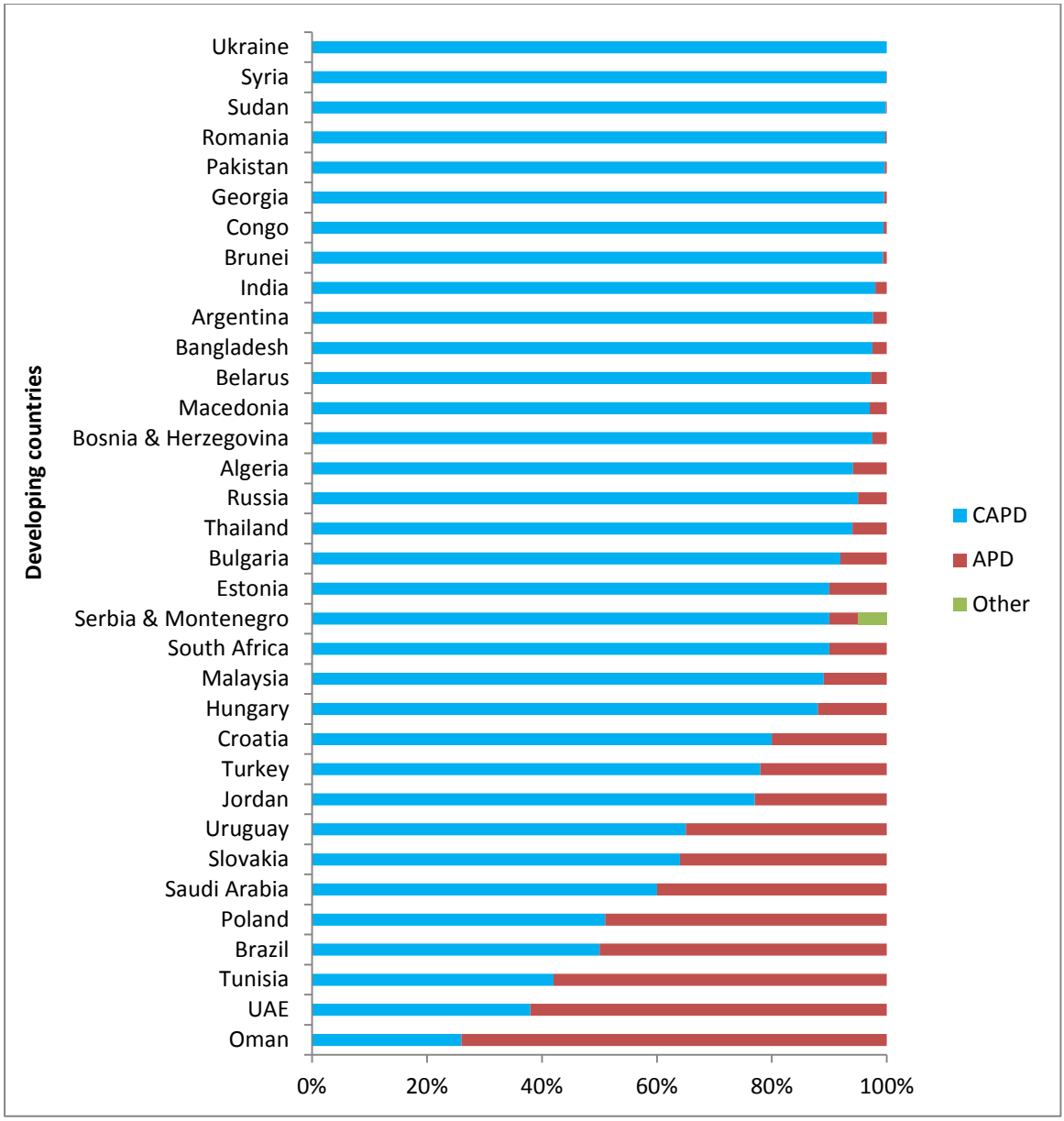

Figure 2.10: The types of peritoneal dialysis used in developing countries (adapted from Jain *et al.*, 2012)

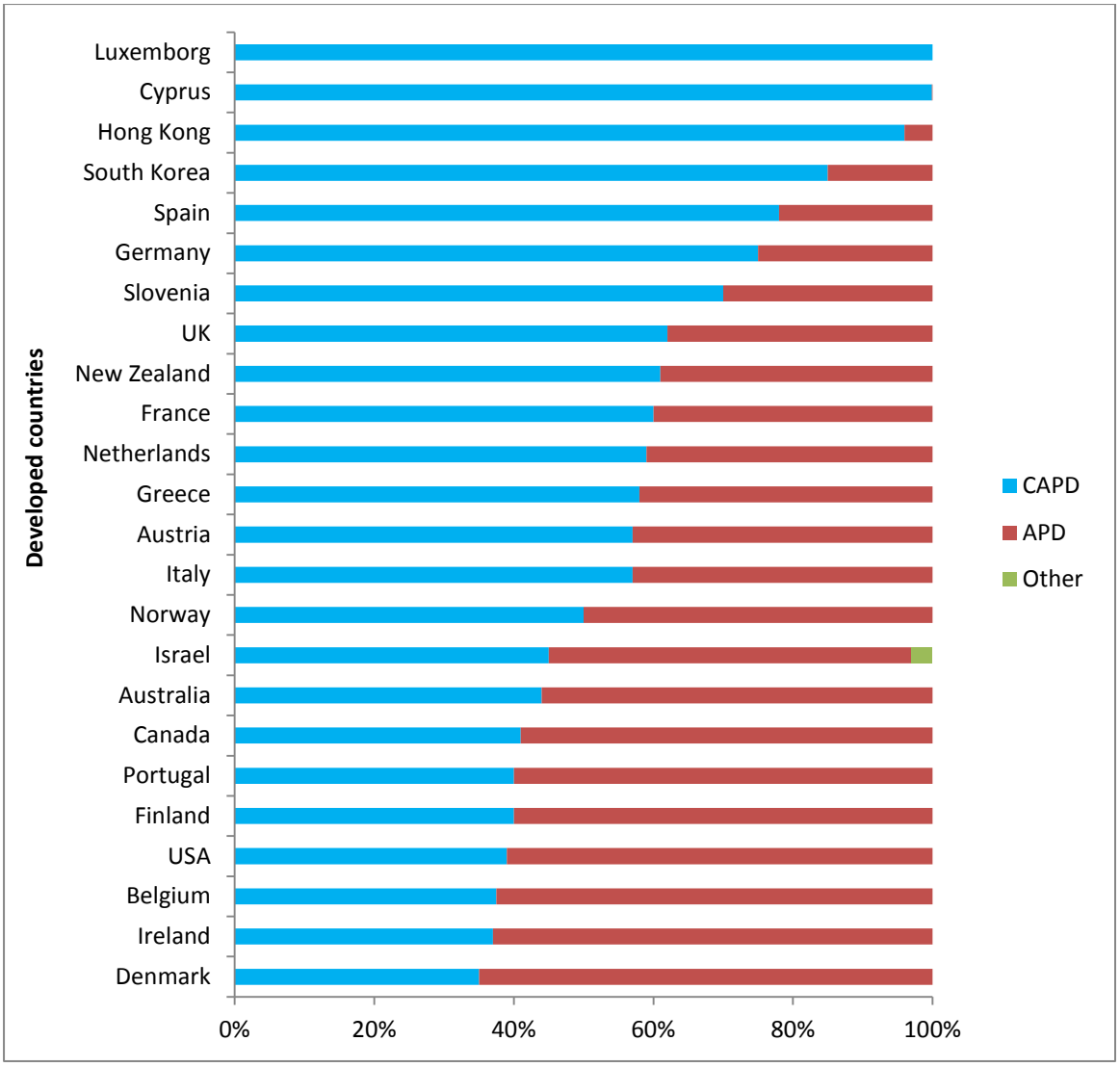

Figure 2.11: The types of peritoneal dialysis used in developed countries (adapted from Jain *et al.*, 2012)

Patients need sufficient storage space for the dialysate bags; and should have hand washing facilities available in order to qualify to receive PD, according to the dialysis protocol (Moosa *et al*., 2006). The low prevalence of patients on PD in Northern Africa are largely attributed to rural setting, unsuitable living circumstances, limited access to improved sanitation and safe water sources, and the limited number of nephrologists (Abu-Aisha & Elamin, 2010). Thus an adequate standard of treatment and care is required for these patients, which can be managed effectively with the limited resources available (Moosa *et al*., 2006).

As with HD, three processes take place during PD: osmosis, diffusion and ultra filtration (Fresenius Medical Care, nd: Online). Osmosis carries waste products from the blood through the peritoneal membrane and into the more concentrated dialysate (Wilkens, Juneja & Shanaman, 2012).

After allowing adequate time for this exchange to take place, the PD dialysate is drained out of the peritoneal cavity into a waste bag, and replaced by fresh dialysate (Schrier, 2009). Varying concentrations of dialysate can be used so that different volumes of water may be removed with each dialysis exchange, as a result of ultra filtration combined with osmosis (Kalra, 2012).

In Africa, only SA and Kenya manufacture dialysis solutions (Abu-Aisha & Elamin, 2010). The *Dan Baxter Company* in the USA, made the first commercial dialysis solution in 1959, and these solutions have not significantly changed since then (Alam & Krause, 2014). The first PD solutions were packaged in glass bottles, but are now commercially available in different sized collapsible plastic bags (Alam & Krause, 2014). The various sizes available for the glucose containing bags are 1500ml, 2000ml, 2500ml and 3000ml (Baxter Health Care, 2012).

The constituents of the dialysate can be divided into osmotic agents, buffers and electrolytes (Alam & Krause, 2014). Osmotic agents are used for fluid removal in patients as osmotic agents are hyperosmolar and thus allow net water removal by altering the osmotic pressure gradient between the PD solution and plasma water (Alam & Krause, 2014). Initial PD solutions were saline solutions, but dextrose has been commonly used as the osmotic agent since the 1940s (Alam & Krause, 2014). Dextrose was used as an osmotic agent with added lactate to lower the pH to 5.2 and thus prevent carmelisation during heat sterilisation of the dialysis solution (Mehrotra & Boeschoten, 2009).

There are three different dextrose monohydrate concentrations (1.5 %, 2.5% and 4.25%) available on the market, which can be combined for different outcomes in patient care (Mehrotra & Boeschoten, 2009). Optimal blood pressure control and the patient's dry weight can be achieved by alternating the different concentrations of dextrose-containing solutions (Alam & Krause, 2014). The advantages of using dextrose as an osmotic agent, is that it is cheap, safe, easily available and nephrologists are comfortable using these solutions (Alam & Krause, 2014). Dextrose, however, is not the ideal osmotic agent, as it is easily absorbed and leads to short-lived ultrafiltration (Han *et al*., 2012). Hyperglycemia, hyperinsulinemia, hyperlidemia and weight gain are thus experienced when large amounts of glucose are absorbed (Han *et al*., 2012)

An icodextrin peritoneal dialysate bag (also known as *Extraneal*) is a glucose polymer bag that has been used in clinical trials since the early 1990s to allow sustained ultrafiltration during the long dwells (Mehrotra & Boeschoten, 2009). It allows increased peritoneal clearance and increased sodium removal during automated peritoneal dialysis (Posthuma *et al.,* 1997).

An amino acid bag (also known as *Nutrineal*) is a 1.1% amino acid–containing solution with an ultrafiltration capacity equivalent to a 1.5% dextrose peritoneal dialysis bag (Mehrotra & Boeschoten, 2009). *Nutrineal* is similar to *Extraneal* as it contains no glucose and is more biocompatible to the peritoneal membrane than the conventional dialysates (Chang *et al.*, 2007). *Nutrineal* is indicated for use in malnourished or diabetic patients, and/or patients with recurrent peritonitis (Alam & Krause, 2014). Nutritional benefits of this amino acid containing dialysate is seen if the Nutrineal bag is administered during the evening, combined with the normal glucose containing bags during the day, while optimal nutrition isd also provided (Tjiong *et al.*, 2009).

Xylitol containing PD solutions have been tested in patients with diabetes mellitus and preliminary research found that it helped decrease metabolic complications associated with diabetes mellitus and blood glucose levels (Alam & Krause, 2014). These PD bags are, however, not used in the clinical setting, due to several potential serious side effects, such as lactic acidosis, hyperuricemia, carcinogenicity, and poor liver function (Alam & Krause, 2014).

Three different agents (lactate, acetate and bicarbonate) have been used as buffers in PD solutions to control acidosis (Feriani, 1996). Lactate is generally safe to use and is commercially available in concentrations of 35 mmol/L and 40 mmol/L (Alam & Krause, 2014). Acetate controls metabolic acidosis of chronic uraemia, but leads to poor ultrafiltration (Alam & Krause, 2014). Bicarbonate controls acidosis, but it is not compatible with calcium- and magnesium-containing PD solutions (Alam & Krause, 2014). Two separate bags are thus mixed together at the time of infusing the solutions (Alam & Krause, 2014). Different concentrations of bicarbonate are mixed with lactate, with variable results (Alam & Krause, 2014).

Commercially available PD solutions contain electrolytes (sodium, magnesium, calcium and chloride) (Alam & Krause, 2014). Potassium and minerals like iron pyrophosphate can also be added to the PD solution (Alam & Krause, 2014). The variety of formulations allow health care professionals to prescribe suitable PD solutions, based on the patient's individual electrolyte and metabolic profile and thus offers a tailored prescription (Alam & Krause, 2014).

A lower sodium concentration (130 – 137 mmol/L) dialysate is usually chosen for PD solutions to prevent hypernatremia (Alam & Krause, 2014).The magnesium concentrations in PD solutions vary from 0.5 mEq/L to 1.5 mEq/L (Alam & Krause, 2014).

Hypermagnesemia are often seen in patients receiving PD (persistently elevated magnesium levels may cause bone disease), thus t he 0.5 mEq/L concentration is more commonly used to optimise the serum magnesium concentration (Alam & Krause, 2014). The optimal calcium concentration needed in PD solutions is unclear (Alam & Krause, 2014). Many dialysis clinics use low calcium concentration PD solutions (1.25 mmol/L), helping in the treatment of hyperphosphatemia; together with calcium-containing phosphate binders (Alam & Krause, 2014). Hypercalcemia is common in patients receiving CAPD when using the 1.75 mmol/L calcium PD solution (Alam & Krause, 2014).

CAPD has many advantages compared to HD (Moosa *et al*., 2006), including convenience for the patient - as the patient can continue working, no vascular access needed -, flexibility, and fewer cardiovascular complications (Moosa *et al*., 2006). Furthermore, patients in rural areas do not have to travel to the dialysis centre and patients receiving CAPD can dialyse every day as opposed to patients on HD who dialyse three times per week for a period to four hours at a time. CAPD also gives the opportunity for a better exchange (Schrier, 2009).

Cost comparison in many well documented studies overseas have shown that CAPD is cheaper to maintain than HD (Berger *et al.,* 2009; Klarenbach & Manns, 2009; Rodriguez-Carmona A *et al.*, 1996; Nebel, Finke & Renner, 1991). A retrospective cohort conducted over three years showed that the median healthcare costs over the 12-month follow-up period were US$ 43,510 higher in patients receiving HD than in the patients receiving CAPD (Berger *et al.,* 2009). These higher costs were largely due to differences in the cost of inpatient care and medications as patients receiving HD have an increased use of erythropoietin-stimulating agents (Berger *et al.,* 2009). Other costs included emergency and other outpatient consultations; and hospitalisations (Berger *et al.,* 2009). Interestingly however, a cost comparison has shown that in SA, CAPD is more expensive than HD, amounting to US $12000 and US$ 7000 respectively (Abu-Aisha & Elamin, 2010). These figures were estimates provided by six experts in Sub-Saharan Africa in response to an e-mail-based survey, in which the items of cost analysis are not indicated in the study (Abu-Aisha & Elamin, 2010).

Disadvantages of CAPD include concerns of starting CAPD in certain patients, such as patients not being physically or psychologically able to do CAPD exchanges, limited storage space and limited hand washing facilities, significant previous abdominal surgery, obese patients and patients with a hernia (Moosa *et al*., 2006).

When patients need to start RRT, it is important to consider the clear advantages and disadvantages of HD and CAPD. Patients receiving CAPD can enjoy longer periods of time independent of a dialysis clinic.

2.9 Assessing nutritional status of patients receiving CAPD

The prevalence of malnutrition and wasting is common in CRF patients (Calvo *et al.,* 2002; Schreiber, 2001; KDOQI, 2000; Kooman *et al.,* 1992), particularly in patients receiving CAPD (Abdu *et al.,* 2011; Naicker, 2003; Burkart, 2002; Flanigan *et al.,* 1998; Young *et al.*,1991), and is associated with higher rates of morbidity and mortality (Pifer *et al.,* 2002; Jansen *et al.,* 2001; KDOQI, 2000; Avram *et al.,* 1996; Canada-United States of America (CANUSA) Peritoneal Dialysis Study Group, 1996). As discussed before, etiological factors contributing to PEW in patients with ESRD before the commencement of dialysis include anorexia, inflammation, metabolic acidosis, endocrine disorders, co-morbidities, dialysis and psychosocial problems (KDOQI, 2000; Stenvinkel *et al.,* 1999).

When the patient starts on CAPD, the most critical issue is to ensure an adequate nutritional intake, as CAPD patients lose more protein through dialysis than patients receiving HD, leading to hypoalbuminemia. CAPD patients therefore have higher protein requirements than patients receiving HD (Schrier, 2009). Peritoneal solutions contain glucose, which is absorbed through the peritoneal membrane on a daily basis (Schrier, 2009) and therefore these patients initially, in the first 12 to 18 months, gain weight (Schrier, 2009). An additional long term physiological change however, occurs where many patients seem to lose lean body mass, but the mechanism is unclear when relating it to the adequacy of dialysis or underlying inflammatory processes (Schrier, 2009). The CANUSA study showed a reduced patient survival and increased hospitalisation in patients with a poor nutritional status (Mitch & Ikizler, 2010).The incidence of mortality increases with hypoalbuminemia (Fouque *et al.*, 2007; Kopple, 1994).

Nutritional status in patients with ESRD has been highlighted as a very important issue during the past few years (Mitch & Ikizler, 2010). Currently KDOQI recommends that a patient's nutritional status should be assessed using a multi-dimensional approach, as the optimal protocol to diagnose and monitor the response to nutrition intervention has not yet been identified (KDOQI, 2000). The parameters with nutritional relevance include: clinical assessment; assessment of body weight, body composition and food intake; biochemical assessment; and psychosocial evaluation (KDOQI, 2000).

Ideally a marker to determine nutritional risk in a patient with ESRD should be inexpensive, reproducible, easily performed and not influenced by other factors such as gender, age and systemic diseases (KDOQI, 2000).

This marker should also not be affected by the patient's underlying disease or inflammatory status (Mitch & Ikizler, 2010) and needs to accurately predict the outcomes of the patient (KDOQI, 2000). No such single nutritional marker has been identified in patients with CRF (Mitch & Ikizler, 2010; KDOQI, 2000).

2.9.1 Anthropometric measurements

Simple measurements such as a patient's weight, body mass index (BMI), mid upper arm circumference (MUAC), and tricep skin fold (TSF) are easy anthropometric measurements to perform and interpret (Mitch & Ikizler, 2010). These measurements are, however, insensitive to changes in the patient's body composition, but can be useful in conjunction with other assessment measurements (Mitch & Ikizler, 2010).

2.9.2 Subjective Global Assessment (SGA) nutrition assessment tool

The Subjective Global Assessment (SGA) nutrition assessment tool is a reliable predictor of cardiovascular risk in both male and female patients with ESRD (KDOQI, 2000). Despite different opinions regarding the validity of SGA nutrition assessment tool in the CAPD population, it is recommended by KDOQI (KDOQI, 2000) for clinical assessment of nutritional status. The use of SGA nutrition assessment tool in patients receiving CAPD was validated by Enia *et al. (*1993) and many large prospective studies have shown that the SGA nutrition assessment tool reliably predicts poor outcome in dialysis patients (Pifer *et al.,* 2002; KDOQI, 2000; Canada-USA (CANUSA) Peritoneal Dialysis Study Group, 1996). The SGA nutrition assessment tool is easily accessible, cheap, quick to complete, and has a strong correlation with mortality.

The SGA nutrition assessment tool is scored on a seven point Likert scale and evaluates four topics, namely weight change, anorexia, subcutaneous tissue and muscle mass (KDOQI, 2000). Once the score is tallied, the patients are characterised into one of three categories, namely well nourished, mild/moderately malnourished, or severely malnourished patients (Mitch & Ikizler, 2010). The SGA nutrition assessment tool is easily available, cheap, quick to complete, and has a strong correlation with mortality. It evaluates the patient in a subjective and objective manner, as the second part to the evaluation consists of a physical examination of the patient (KDOQI, 2000).

This assessment tool can be applied by doctors, nurses or dietitians and can be done on routine visits to the center (KDOQI, 2000). It forces the health care professional to look at the patient holistically (KDOQI, 2000). No data indicates how often this should be done, but the KDOQI guidelines state that, after the first six months of treatment, it should be performed every four months (KDOQI, 2000).

The SGA nutrition assessment tool is however, not a sensitive or a reliable predictor of the degree of malnutrition (Mitch & Ikizler, 2010:197). In a South African study it was shown that 60% of patients had a BMI above the normal range, despite only 42% being classified as well-nourished using the SGA nutrition assessment tool (Abdu, Ladeira & Naiker, 2011). This supports the findings of Cooper *et al.* (2002) that the SGA nutrition assessment tool may not reliably predict protein malnutrition as it may not differentiate malnourished patients from those with a normal nutritional status.

2.9.3 Biochemical measures

2.9.3.1 Serum albumin

The most frequently used measurement in a patient with CRF is serum albumin levels (Mitch & Ikizler, 2010). The serum albumin measurement is easily accessible, easy to perform and affordable (Mitch & Ikizler, 2010; Kalantar-Zadeh *et al*., 2011). Prealbumin has a shorter half-life than albumin and is thus more sensitive to shorter term changes in visceral protein stores than serum albumin (Kalantar-Zadeh *et al.,* 2011). The disadvantage of using serum albumin is that it decreases in response to inflammation, as it is a negative acute phase reactant. Patients receiving CAPD are at risk of infection, and thus increased inflammation markers, if there are limited hand washing facilities in the patient's house, or if proper hygiene is not followed (Moosa *et al*., 2006).

Low serum albumin is the strongest measure of mortality in patients with CRF (Lacson *et al.,* 2009), even when comparing it to other risk factors associated with a higher mortality, such as hypertension, hypercholesterolemia, diabetes mellitus and obesity (Lacson *et al.,* 2009). Interestingly, studies have found that a change in serum albumin of a mere 1g/L over a time span of a few months, is associated with an increase or decrease in survival rate (Kalantar-Zadeh *et al*., 2004). This demonstrates the highly incremental and linear relationship between serum albumin and mortality rates, while the other predictors of mortality in CKD demonstrate a U-shaped or J-shaped survival association (Kalantar-Zadeh *et al*., 2005; Lacson *et al.,* 2009). Higher serum albumin and associated improved survival, has been reported in a dialysis center among patients receiving superior care compared to inferior care (Lacson *et al.,* 2009).

2.9.3.2 Cholesterol

The KDOQI Guidelines state that serum cholesterol is a valid and clinically useful marker of protein energy nutritional status in patients receiving HD (KDOQI, 2000). Interestingly, the relationship between low serum cholesterol and increased mortality observed in the patients receiving HD, has not been observed in the CAPD population (Avram *et al.,* 1995; De Lima *et al.*, 1995; Lowrie *et al.*, 1995).The predialysis serum cholesterol may be a useful screening tool for detecting chronically inadequate protein-energy intakes.

Patients with a low to normal (< 3.8 to 4.6 mmol/L) non-fasting serum cholesterol have higher mortality rates than those with higher cholesterol levels (Lowrie, Huang & Lew, 1995; Avram *et al.,* 1995). Serum cholesterol is an independent predictor of mortality in patients receiving HD (Lowrie, Huang & Lew, 1995). The U-shaped or J-shaped relationship between serum cholesterol and mortality is explained by the increased risk for mortality as the serum cholesterol rises above 5.2 to 7.7 mmol/L (Lowrie, Huang & Lew, 1995) or falls below 5.2 mmol/L (Avram *et al.,* 1995; Goldwasser *et al.*, 1993). This relationship between low serum cholesterol and increased mortality has not been observed in the CAPD population (Lowrie, Huang & Lew, 1995; Avram *et al.,* 1995; De Lima *et al.*, 1995). This could be due to small study sample sizes, or may be explained by the greater energy intakes in patients receiving CAPD through the obligatory glucose absorption from the bags, which lead to hypertriglyceridemia. One study in patients receiving CAPD found that a higher serum cholesterol concentration (> 6.4mmol/L) was associated with increased mortality (Iseki *et al.*, 2002).

Cholesterol can be affected by the same co-morbidities, such as inflammation (that could affect the patient's serum albumin) (Cano *et al.*, 1988). However, one study showed no difference in serum cholesterol in patients receiving CAPD whose serum albumin level was below 35 g/L and more than 35 g/L respectively (Han *et al.*, 1996). Cardiovascular disease though, is the most common cause of death in patients receiving dialysis (Schrier, 2009). Aggressive treatment of lipid disorders should be standard in treating patients and preventing death, although there are no outcome studies available (Schrier, 2009).

2.9.4 Assessing protein intake in patients with CKD

2.9.4.1 24-Hour Recall

The measurement of dietary intakes of individuals and groups is central to nutrition research (Steyn & Labadorius, n.d: Online). Individual dietary assessment methodologies include the 24-hour recall, diet history, weighed and estimated food records and food frequency questionnaires.

The main use of a single 24-hour recall is to describe the average dietary intake of groups of individuals (Steyn & Labadorius, n.d: Online). There are many advantages of the 24-hour recall as an individual dietary assessment methodology. The main advantage of the 24-hour recall is the speed and ease of administration (Nelson & Bingham, 1997). the 24h recall has been used in various large scale and national surveys and has also been used extensively in the United States, since 1971 in the National Health and Nutrition Examination Survey (NHANES I, II and III) (Thompson & Byers, 1994).

Another advantage of the 24-hour recall is that no literacy is required from the participant, as the interviewer administers and fills in the responses, requiring only verbal answers from the participant (Nelson & Bingham, 1997). This method is thus used across a wide range of populations (Nelson & Bingham, 1997). The burden on the participant is small, as the interview generally takes about 20 minutes to complete (Nelson & Bingham, 1997). Participants usually recall most of their dietary intake from the previous day due to the immediacy of the 24-hour recall (Thompson & Byers, 1994). This assessment method does not interfere with dietary behavior, as the recall takes place after the food has been consumed (Thompson & Byers, 1994)

Disadvantages of using the 24-hour recall, include the fact that a single 24-hour recall record may not represent the usual diet of an individual; while it is well known that participants with lower observed intakes tend to over-report, and those with higher observed intakes, tend to under-report their past dietary intake (Ferguson *et al*., 1995; Gewa, Murphy & Neumann, 2009). Furthermore, one study showed over 60% of fruits and snacks were omitted from the 24-hour recall (Ferguson, Gibson & Opare-Obisaw, 1994).

Therefore, the 24-hour recall should be repeated, preferably on nonconsecutive days (Steyn & Labodarius, n.d: Online; Thompson & Byers, 1994). Various factors that need to be taken into consideration for a good quality control 24-hour recall includes: a detailed protocol of administration, appropriate training of the administrators of the questionnaire, duplicate collection of some of the recalls in the study period, and the use of a computerised data system for nutrient analyses (Steyn & Labodarios, n.d: Online; Thompson & Byers, 1994).

The Nordic Co-operation Group of Dietary investigators have recommended specific procedures when using the 24-hour recall method, which include: a quiet, relaxed atmosphere when the recall is conducted; no advance warning of the interview given to the participant to prevent changed dietary intake; the use of dietary aids to assist the identification of portion size; equal distribution of interviews over the days of the week; and the use of open-ended forms with pre-coded foods to facilitate the process and decrease errors in transcription (Steyn & Labodarios, n.d: Online)

2.9.4.2 Normalised protein nitrogen appearance (nPNA)

Normalised protein nitrogen appearance (nPNA) is a valid and clinically useful measure of net protein degradation and protein intake in patients receiving dialysis (Mitch & Ikizler, 2010). It is an indirect method for estimating dietary protein intake (KDOQI, 2000) and an accurate reflection of dietary protein intake in metabolically stable patients (Mitch & Ikizler, 2010).

There are, however, many limitations in using the nPNA in the assessment of nutritional status in patients receiving CAPD. The nPNA approximates protein intake only when the patient is in a steady state i.e. neither in anabolic nor in catabolic state (Abdu, Ladeira & Naiker, 2011). A catabolic patient will have an elevated serum urea, and the reason for this might not necessarily be high protein intake, but may be due to other factors (Mitch & Ikizler, 2010). Rapid changes in the nPNA are caused by changes in protein intake, therefore it fluctuates on a daily basis and one nPNA measurement may not reflect usual protein intake (Abdu, Ladeira & Naiker, 2011). Normalising PNA to body weight can also be inaccurate in obese, malnourished, and oedematous patients (Abdu, Ladeira & Naiker, 2011).

2.10 Supplementation of malnourished patients with CKD

PEW increases mortality rates in patients with CKD and therefore dietary and non-dietary interventions are vitally important to improve patients' nutritional status (Kalantar-Zadeh et al., 2011). Literature indicates that PEW can be corrected by appropriate diet and nutritional supplements that target dietary protein intake (Kalantar-Zadeh et al., 2011).

Several factors influence supplementation regimes in patients receiving PD (Kalantar-Zadeh *et al.,* 2011). The peritoneal solutions contain glucose, which is absorbed by the patients on a daily basis (Schrier, 2009). This constitutes approximately 1260 – 2520 kJ (300-600 kCal) per day, additional to the dietary intake (Schrier, 2009). Patients thus often have a decreased oral energy intake (Kopple & Mehrotra, 2003).

This may depend on the peritoneal transport rate and dialysis prescription (Kopple & Mehrotra, 2003). Patients receiving maintenance dialysis who are unable to meet their protein and energy requirements with food intake for an extended period of time, should receive nutritional support (KDOQI, 2000). If all the patient's complications with dialysis have been resolved, and there is still no increase in the patient's appetite and food, nutritional supplementation may be necessary (Bossola *et al.,* 2005).

Kantar-Zadeh *et al.* (2011) recommend that in-centre meals or oral supplements are an inexpensive method that may improve patients' quality of life as well as their survival. As mentioned earlier, patients typically lose more protein while receiving CAPD than HD, and thus have a higher nutritional protein requirement (Westra *et al.,* 2007). An average of five to seven grams of protein is lost per day through the dialysis, and these losses are significantly increased during episodes of peritonitis (Westra *et al.,* 2007). Inadequate intake, as well as intolerance to oral supplements, may be caused by slow gastric emptying associated with the intraperitoneal administration of the dialysate (Van Vlem *et al*., 2002). Other factors which may contribute to wasting, include anorexia (due to nausea, emesis, medication side effects, uremia, inflammation and under-dialysis); inflammation (due to comorbidities and related to dialysis procedures); metabolic acidosis; endocrine disorders; and psychosocial factors (depression, low physical activity, loneliness and poverty) (KDOQI, 2000).

Positive results in serum albumin levels have been reported with protein supplementation studies. Eustace *et al.* (2000) supplemented 47 patients receiving HD and PD with 3.6 grams essential amino acids, with meals three times daily for 3 months and resulted in an increased serum albumin of 2 g/dL (P=0.02). Aguirre-Galindo *et al* (2003) also found a positive result with protein and energy supplements in their group of 100 patients receiving CAPD. Malnourished patients received 1.4 g/kg protein powder and 35 kCal/kg per day for a period of four months (Aguirre-Galindo *et al.,* 2003). The group that was supplemented with 50% calcium casseinate and 50% natural protein had a constant small increase in serum albumin levels: 0.0019 g/L in every month of the trial (P<0.01) (Aguirre-Galindo *et al.,* 2003). González-Espinoza *et al* (2005) performed an open label controlled trial with an egg albumin based supplement with a six month follow up in 28 patients receiving CAPD. This trial used 15g twice daily egg based supplements, together with nutritional concenlling from a renal dietitian (González-Espinoza *et al.,* 2005). The most important predictors of an increase in serum albumin concentrations in their trial was an egg based oral nutritional supplement and an increase in daily protein intake (P<0.05) (González-Espinoza *et al.,* 2005).

Certain generalisations have been made about certain aspects about supplementation in these patients. Oral supplements can increase the total daily energy and protein intake of patients receiving CAPD (Boudville, Rangan & Moody, 2003) by providing an additional 29.4 – 42 kJ/kg/day (seven to 10 kCal/kg/day) and 0.3-0.4g/kg per day of protein (Kalantar-Zadeh et al., 2011). Kalantar-Zadeh *et al.,* (2011) suggested that oral supplements should be given to patients two to three times per day, preferably one hour after meals in order to meet the recommended dietary energy and protein requirements. Improvement in nutritional status have been reported in patients who are compliant and tolerate the dietary supplements (González-Espinoza *et al*., 2005; Teixidó-Planas *et al.*, 2005; Aguirre-Galindo *et al.,* 2003; Shimomura, Tahara & Azekura, 1993). Some evidence suggests that orally supplemented essential amino acids may be beneficial to patients with significant hypoalbuminea, but more studies are needed to warrant any recommendation (Bossola *et al.,* 2005)

Obesity is a concern in today's society, which may lead to hypertension, diabetes mellitus and CRF, which leads to a raised mortality (Kalantar-Zadeh *et al.,* 2004). In the patient with CRF, PEW is more of a concern leading to a higher mortality and the most important approach when supplementing these patients, is addressing the most life threatening complication that the patient is experiencing (Kalantar-Zadeh *et al.,* 2004). This is demonstrated in an example where the patient will die of a short term consequence such as PEW, before dying of risk factors associated with obesity (Kalantar-Zadeh *et al.,* 2004). This is known as the *'time discrepancy'* hypothesis (Kalantar-Zadeh *et al.,* 2004). This hypothesis is demonstrated in two randomised controlled trials where a cholesterol lowering diet in patients with hyperlipidemia had no effect on their survival (Fellström *et al*., 2009; Wanner *et al*., 2005). Kato *et al.* (2010) found that serum albumin was far more superior as a mortality predictor than inflammatory markers or intima media thickness of the common carotid artery in a ten year cohort study with 206 patients receiving HD. One study also suggests that controlling serum phosphate levels through strict dietary protein restrictions may cause increased mortality (Shinaberger *et al*. 2008), especially in patients with a low serum albumin and decreased normalised protein catabolic rate (Shinaberger *et al*., 2008). This could explain the contradictory observations of increased survival of patients who did not abide to strict rules of not eating any food during dialysis therapy (Kalantar-Zadeh *et al.,* 2005).

If nutritional supplements are not effective in patients receiving dialysis, other pharmaceutical therapies may be used in conjunction with diet and dietary supplements, such as appetite stimulants, anabolic hormones, anti-inflammatories and intradialytic parenteral nutrition.

2.11 Adequacy of dialysis

Peritoneal transport status is one of the main determinants of dialysis adequacy and dialysis-related complications in ESRD patients receiving CAPD (Sezer *et al.,* 2005). The patient's transport status is very useful for prescribing an individualised medical care plan (Moosa *et al.,* 2006). The recommended dose of dialysis that a patient receives can be calculated by evaluating the patient's weekly kinetic modelling (Kt/V) or creatinine clearance (Moosa *et al.,* 2006).

The Kt/V is a measurement of the removal of urea from the patient's blood over time; K refers to the urea clearance of the dialyser, t to the length of time of dialysis, and V to the patient's total body water volume; (Wilkens, Juneja & Shanaman, 2012). The residual renal function plays an integral part in the patient's ability to achieve adequate clearance (Schrier, 2009). Measurement of Kt/V in patients receiving CAPD involves the measure of both the renal and peritoneal urea clearances through the determination of the serum urea, as well as the 24 hour dialysate and urine urea. The urea distribution volume (V) is usually estimated either using a fixed percentage of body weight or using anthropometric formulae such as the Watson's formula (Watson, Watson & Batt, 1980). underdialysis contributes to PEW (KDOQI, 2006). National guidelines from the United States, Canada, and Europe no longer recommend the use of creatinine clearance as the measure of dialysis adequacy (KDOQI, 2006; European Best Practice Guidelines for peritoneal dialysis, 2005). However, it is mentioned that this measurement may still be used to monitor the 24 hour dialysate and urine creatinine removal as the creatinine clearance is an estimation of muscle mass and a reflection of phosphate clearance in PD (KDOQI, 2006; European Best Practice Guidelines for peritoneal dialysis, 2005).

The South African target goals for Kt/V is at least 2.0, and that for creatinine clearance at least 70L/week/1.73 m^2 (Moosa *et al.,* 2006). The US Guidelines recommended goal for Kt/V is at least 1.7 (Schrier, 2009). The International Society for Peritoneal Dialysis (ISPD) has also recommended that the total (renal + peritoneal) Kt/V urea should not be less than 1.7 at any time (Lo *et al*., 2006).

2.12 Extent of the problem in SA

SA has experienced an increase in patients with ESRD over the past years who have been receiving dialysis (Moosa *et al*., 2006). Therefore the need for dialysis facilities, increased awareness of renal failure, and proper diagnosis of patients in private and state institutions, are also increasing (Abu-Aisha & Elamin, 2010; Moosa *et al.*, 2006). This level of patient care relies on costly support by health systems (Moosa *et al*., 2006).

A shortage of trained health care professionals in this field in SA further puts strain on the availability of adequate and timely treatment options for patients (Moosa & Kidd, 2006). Therefore efforts need to optimise CRF therapy (Naiker, 2003). On a primary health care level, screening for, and managing of conditions such as hypertension and diabetes mellitus, which are the leading causes of renal damage (Schrier, 2009), is vital to prevent renal failure (Naiker, 2003).

According to the South African Renal Society guidelines, the nutritional status of patients receiving CAPD should be assessed on an ongoing basis, in conjunction with the patient's Kt/V and creatinine clearance measurements, using the nPNA and SGA nutrition assessment tool (Moosa *et al*., 2006). This is in line with the NKF guidelines and should be done often enough to detect changes in the patient and sufficient time to manage and treat complications (KDOQI, 2000).

2.13 Conclusion

The main function of the kidney is to maintain homeostatic balance of fluids, electrolytes and organic solutes (Wilkens, Juneja & Shanaman, 2012). ESRD can result from a wide variety of different diseases; and non-modifiable risk factors for ESRD are ethnicity and age, whereas modifiable factors that contribute to the decline of GFR, and associated albuminuria, include hypercholesterolemia, obesity, smoking, dietary salt intake, oral contraceptives and hormone replacement therapy (Ide & Akani, 2011).

Advanced ESRD presents with many problems related to the kidney's inability to excrete waste products, leading to uremic syndrome, PEW, altered electrolyte and hormonal responses, acid-base disturbances and renal osteodystrophy (Wilkens, Juneja & Shanaman, 2012). Two options of RRT are available in SA, namely HD and CAPD and is initiated in South African patients with a GFR of less than 15ml/minute; and if the patient has one or more signs or symptoms of uremia, fluid overload refractory to diuretics, poorly controlled blood pressure, or evidence of malnutrition (Moosa *et al*., 2006).

The prevalence of malnutrition and wasting is significant in patients receiving CAPD (Abdu *et al.,* 2011; Naicker, 2003; Burkart, 2002; Flanigan *et al.,* 1998; Young *et al.*,1991) as well as common in patients with CRF (Calvo *et al.,* 2002; Schreiber, 2001; KDOQI, 2000; Kooman *et al.,* 1992) and this is associated with higher rates of morbidity and mortality (Pifer *et al.,* 2002; Jansen *et al.,* 2001; KDOQI, 2000; Avram *et al.,* 1996; Canada-United States of America (CANUSA) Peritoneal Dialysis Study Group, 1996).

Nutritional status in patients with ESRD has been highlighted as a very important issue during the past few years (Mitch & Ikizler, 2010). Currently KDOQI recommends that a patient's nutritional status should be assessed using a multi-dimensional approach, as the optimal protocol to diagnose and monitor the response to nutrition intervention has not yet been identified (KDOQI, 2000). The parameters with nutritional relevance include: clinical assessment; assessment of body weight, body composition and food intake; biochemical assessment; and psychosocial evaluation (KDOQI, 2000).

Chapter 3: Methodology

3.1 Introduction

In this chapter the methodology is described according to the study design; study population and sample selection; inclusion and exclusion criteria; variables, operational definitions and techniques of socio-demographic information, medical history, CAPD regime, nutritional status parameters (such as anthropometry, SGA nutrition assessment tool, biochemical measures and dietary intake), protein supplementation, and efficacy of dialysis; validity and reliability; statistical analysis; pilot study; study procedure including the roles and responsibilities of health care workers and participants; ethical aspects including ethical approval, informed consent and sponsorship of the protein powder.

The initial baseline assessments took place when the patients came into the renal unit for routine monthly assessments of biochemical measures. The patients were randomised into two groups, according to the randomisation factors as discussed below.. Kalantar-Zadeh *et al* (2011) recommends that all patients with CKD should be assessed on a monthly or quarterly basis to investigate whether PEW is present and offer nutiritional support to those patients who need it. Therefore the duration of three months was chosen for this trial to investigate whether supplememntation with a protein powder would have an effect on nutritional status over this period of time.

3.2 Methodology

3.2.1 Study design

A randomised controlled clinical trial was conducted.

3.2.2 Study population and sample selection

At the time of the study Frere Hospital was treating 32 patients on HD and 28 patients on CAPD. The numbers of patients receiving CAPD had increased over the preceding few years at this hospital. Furthermore, the percentage of patients with CKD receiving CAPD at Frere Hospital at the time of the trial (September 2012 to December 2012) was higher (at 47%) than the reported South African national percentage of patients with CKD receiving CAPD (32%).

The study population consisted of all patients on CAPD at the renal unit of Frere Hospital in East London (Buffalo City District) at the time of the trial. All patients were informed by the researcher about the trial during baseline nutritional assessment, and given the opportunity to partake. The whole group was subsequently recruited for the trial. Although the sample size was small, it reflects the number of patients in SA with CKD who receive CAPD (32%), and is in line with similar clinical trials around the world, which generally tend to also have smaller sample sizes (Abu-Aisha & Elamin, 2010).

One participant in the control group died before the intervention trial started; one participant (8.3%) in the intervention group changed from CAPD to HD during the intervention, and one participant (9.1%) in the control group had transport issues during transport strikes in the EC during December 2012, preventing him from coming to the CAPD dialysis unit. These participants were thus excluded from the final follow-up assessment. See Figure 3.1 below for a diagram of the sample selection.

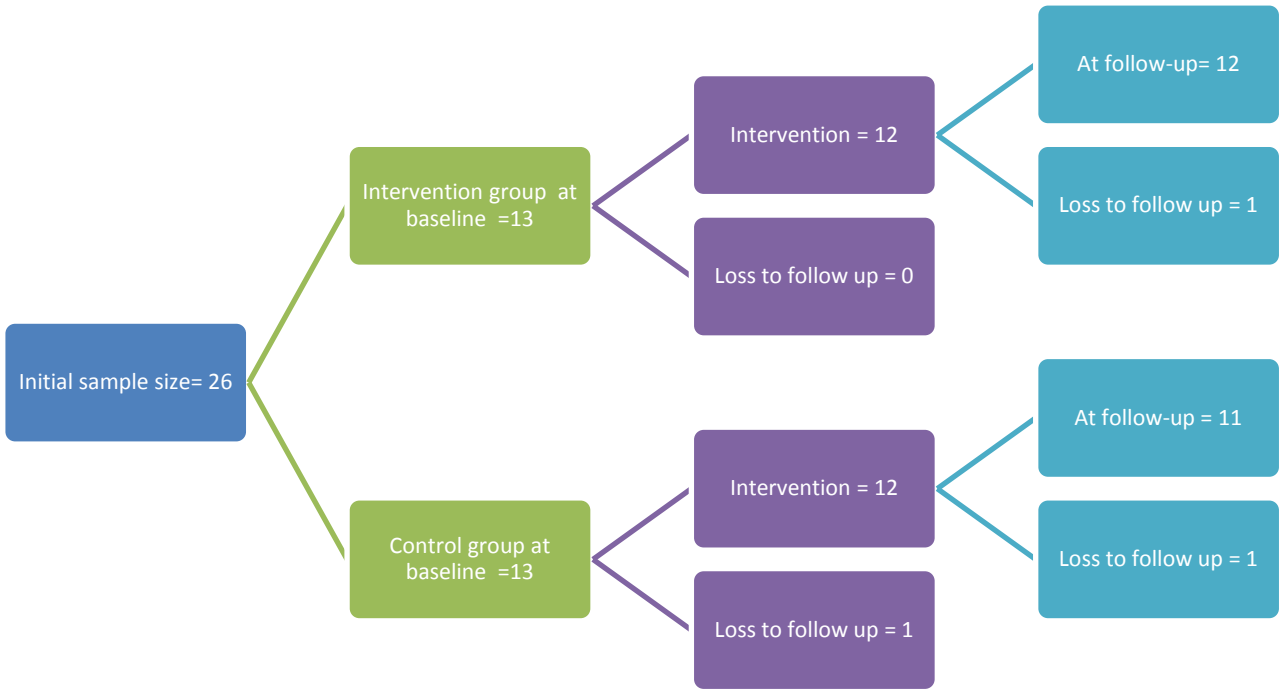

Figure 3.1 Sample selection and loss to follow up

Participants were randomised into two groups based on the median age, gender, median serum albumin levels and median duration of CAPD, as recorded in Table 3.1. Of the entire population of 28 patients treated with CAPD at Frere Hospital, 28 were recruited to the trial. After randomisation, at the baseline assessment, the sample consisted of 13 participants in the experimental group and 13 participants in the control group. One patient in the control group died before the intervention started, thus the control group comprised of 12 participants for the remainder of the trial. .

The randomisation was performed by the Department of Biostatistics of the Faculty of Health Science of the University of the Free State, using randomised lists and random allocation into the two groups. The total population was used for the trial, with no power calculations done for the sample due to the small total population size. The medians were used due to the small total population size. At the time of the study standards of care for the patients receiving CAPD at Frere Hospital entailed that the patients only received CAPD bags according to their needs and did not receive any extra supplements. For the purpose of this trial, the intervention group received *Protifar* powder (a protein supplement), while the control group received the current standards of care which did not include any *Protifar* powder.

Table 3.1: Factors, the combinations of which was used to randomise the trial

	Intervention group	**Control group**
Age (years)	Half of sample size < median age	Half of sample size < median age
	Half of sample size > median age	Half of sample size > median age
Gender	>5 = male	>5 = male
	>15 = female	>15 = female
Serum albumin (g/L)	Half of sample size < median at baseline	Half of sample size < median at baseline
	Half of sample size > median at baseline	Half of sample size > median at baseline
Duration on CAPD (months)	Half of sample size < median duration at baseline	Half of sample size < median duration at baseline
	Half of sample size > median duration at baseline	Half of sample size > median duration at baseline

3.2.2.1 Inclusion criteria

All patients receiving CAPD treated at Frere Hospital in East London, in the BC (Buffalo City) District, who completed the informed consent form and were willing to participate, were included in the trial, and randomised according to median age, gender, median serum albumin and median duration on CAPD into the intervention and control groups as discussed above.

Illiterate patients could be included as the *Speaking Books* Informed Consent Book was used, which explains the concepts of informed consent through various pictures, writing, and verbal communication options .

3.2.2.2 Exclusion criteria

Patients receiving HD and patients receiving CAPD treament at other clinics or hospitals, were excluded from both the intervention and control groups. Patients with any BMI and any AMA catergories were included in this trail, therefore patients with a very high or low BMI and AMA were not excluded from this trial.

3.2.3 Variables and operational definitions

For the purpose of this trial the following variables of participants receiving CAPD were measured, namely socio-demographic information, medical history, CAPD regime, nutritional status (anthropometry, SGA nutrition assessment tool, biochemical measures, dietary intake, protein supplementation) and efficiency of dialysis.

3.2.3.1 Socio-demographic

The following socio-demographic information was gathered for each participant: age, race, gender, area of residence, number of people living with the participant and employment status. These data were captured in Appendix 1.

3.2.3.2 Medical history

The aetiology of the participant's renal failure, existing co-morbidities, and medication (type of medication and dosage) was assessed. This information is captured in Appendix 1. HIV status was not tested or recorded from the files, as it was not an objective. of this trial. In order for patients to be accepted onto the dialysis program in state hospitals in the EC, such as Frere Hospital, they have to test HIV negative and routine follow up testing is done in the dialysis unit.

3.2.3.3 CAPD regimen

The CAPD regimen was classified into the following areas: duration of dialysis, solution type, number of daily exchanges and the presence of a HD line. These data were captured in Appendix 1.

3.2.3.4 Nutritional status of participants receiving CAPD

i. Anthropometry measurements

The standard practice of care at Frere Hospital at the time of the trial was only to record monthly weight. For the purpose of this clinical trial the researcher determined edema-free body weight, measured height, MUAC, TSF and calculated the BMI and AMA, according to the KDOQI Guidelines (KDOQI, 2006). The participant's BMI was calculated by dividing the weight in kilograms by height in meters squared.

The participants were classified into four categories according to BMI, namely being underweight ($\leq$18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2) or obese ($\geq$ 30 kg/m^2).

AMA, which is related to the total body muscle mass, taking the participant's MUAC and TSF into account, was calculated using the Frisancho formula described below (Frisancho, 1981).

$$\text{AMA (mm}^2\text{)} = \frac{(\text{MUAC} - \pi\ \text{TSF})^2}{4\pi}$$

The participants were classified into five categories according to AMA, namely wasted (<5th percentile), below-average muscle mass (5th- 25th percentile), normal muscle mass (50th- 75th percentile), above-average muscle mass (75th- 95th percentile), or high muscle mass (>95th percentile) (Lee 2003). These data were captured in Appendix 2.

ii. SGA nutrition assessment tool

The SGA nutrition assessment tool is a reliable predictor of cardiovascular risk in both male and female renal failure patients (KDOQI, 2000) and it is scored on a seven point Likert scale which evaluated four topics, namely weight change, anorexia, subcutaneous tissue and muscle mass (KDOQI, 2000).

Once the score was tallied, participants were classified into three categories, namely severe malnutrition (rating of one or two in most categories, with significant physical signs of malnutrition), mild/moderate malnutrition (rating of three, four or five in most categories, with no clear sign of normal status or severe malnutrition), or well nourished (rating of six to seven in most categories, with significant and continued improvement) (Mitch & Ikizler, 2010).

The participant's history included a history of weight change, dietary intake, gastrointestinal symptoms lasting longer than two weeks and functional capacity. Physical examination included the loss of subcutaneous fat in four areas (shoulders, triceps, chest and hands), the presence of muscle wasting and the presence of edema in three areas (hands, sacrum and feet). This information was captured in Appendix 3.

iii. Biochemical measures

The following parameters were assessed in each participant: S-albumin, S-sodium, S-potassium, S-phosphate, S-creatinine, S-urea and S-cholesterol levels. These values were categorised as either below normal, normal, or above normal. These parameters were analysed by the National Health Laboratory Service (NHLS), Clinical Pathology Sanas at Frere Hospital. This information was captured in Appendix 4 and was interpreted as described in Table 3.2.

Table 3.2: Biochemical parameters, based on the values used at the NHLS at Frere Hospital

Marker	Below normal	Normal range	Above normal
Serum albumin (g/L)	< 35.0	35.0 – 52.0	> 52.0
Serum sodium (mmol/L)	< 135.0	135.0 – 147.0	> 147.0
Serum potassium (mmol/L)	< 3.3	3.3 – 5.3	> 5.3
Serum phosphate (mmol/L)	< 0.8	0.8 – 1.4	> 1.4
Serum urea (mmol/L)	< 2.6	2.6 – 7.0	> 7.0
Serum creatinine (umol/L)	< 64.0	64.0 – 104.0	> 104.0
Serum cholesterol (mmol/L)	< 5.0	5.0	> 5.0

iv. Dietary intake

Information on the participant's 24-hour recall food intake was obtained, categorised and assessed according to the total energy intake, protein intake (total and high biological value protein intakes), carbohydrate and fat intakes.

This data was compared to the KDOQI (2006) recommended daily intakes patients receiving CAPD, and categorised as inadequate, adequate, or more than adequate nutrient intake. This information was captured in Appendix 5 and described in Table 3.3.

Table 3.3: Dietary intake according to KDOQI recommendations (KDOQI, 2006)

	Inadequate intake	Adequate Intake	Above adequate intake
Energy (kCal/kg)	< 30.0	30.0 – 35.0	> 35.0
Total protein (g/kg)	< 1.2	1.2 – 1.3	> 1.3
HBV protein (%)	< 50.0	50.0	> 50.0
Carbohydrate (% of TE)	< 50.0	50.0 – 60.0	> 60
Fat (% of TE)	< 25.0	25.0 – 35.0	> 35.0

3.2.3.5 Protein supplementation

Participants' protein intake was assessed at baseline. Participants were divided up into two groups, the intervention group received protein powder and the control group received no protein powder (standard care at Frere Hospital currently).

Dosages of supplemented protein vary substantially between trials in patients receiving CAPD; from 29.4 – 42.0 kJ/kg/day (seven to 10 kCal/kg/day), or 0.3-0.4g/kg/day (Kalantar-Zadeh *et al*., 2011). It is suggested that oral supplements should be given to patients two to three times per day, one hour after the meal in order to meet the recommended dietary energy and protein requirements (Kalantar-Zadeh *et al*., 2011). Aguirre-Galindo *et al.,* (2003) supplemented their malnourished patients with 1.4 g/kg protein powder and 35 kCal/kg per day for a period of four months; while González-Espinoza *et al.,* (2005) used 15g twice daily egg based supplements, together with nutritional concenlling from a renal dietitian.

In the current trail, the intervention group was supplemented with protein powder at 50% of daily protein requirements (1.3g/kg/day according to KDOQI Guidelines); therefor each participant's dosage was calculated at 0.65g/kg/day protein, , and given in addition to their usual dietary intake.

Participants in the intervention group received the protein powder, *Protifar,* during the intervention period. Participants took the required protein powder on a daily basis, as it was measured out and packaged in individual dosages for them by the researcher. *Protifar* is a powdered, unflavoured, casein dominant protein supplement, for the dietary management of hypoproteinaemia; and is indicated as a protein supplement for patients who are unable to reach their protein requirement from normal food or drink, or for patients with an increased protein requirement (Nutricia, 2011). *Protifar* has a neutral taste and can therefore be added to sweet or savoury food and drinks, without significantly altering the flavour or texture (Nutricia, 2011).

Protifar is sold in a 225g reseable tin (Nutricia, 2011) and the nutritional composition per 100g is: 1560 kJ energy, 87.2g protein (14g nitrogen), 1.2g carbohydrate, 1.6g fat, 110mg sodium, 140mg potassium, 1350mg calcium and 700mg phosphorous. The compliance of protein powder supplementation was captured in Appendix 6 – 8.

3.2.3.6 Efficiency of dialysis

Efficiency of dialysis was assessed by weekly Kt/V and weekly creatinine clearance. The Kt/V is a measurement of the removal of urea from the patient's blood over time; with K representing the urea clearance of the dialyser, t representing the length of time of dialysis, and V representing the patient's total body water volume; (Wilkens, Juneja & Shanaman, 2012). The residual renal function plays an integral part in the patient's ability to achieve adequate clearance (Schrier, 2009). Measurement of Kt/V in patients receiving CAPD involves the measure of both the renal and peritoneal urea clearances through the determination of the serum urea, as well as the 24 hour dialysate and urine urea. The urea distribution volume (V) is usually estimated either using a fixed percentage of body weight or using anthropometric formulae such as the Watson formula (Watson, Watson & Batt, 1980). It is important to ensure proper and accurate Kt/V measurements as underdialysis contributes to PEW (KDOQI, 2006). The weekly Kt/V is described in formula described below (Moosa *et al.,* 2006) and was captured in Appendix 9.

$$\text{Total Kt} = \text{peritoneal Kt} + \text{renal Kt}$$

$$\text{Kt} = \frac{\text{value of the urea in the 24-hour sample of dialysate}}{\text{serum urea}}$$

$$\text{Weekly Kt/V} = \text{Kt/V} \times 7$$

The Watson formula, which is based on sex, age, height and weight, was used to calculate V in Kt/V (Watson *et al.,* 1980). The Watson formula is included in Table 3.4 (Watson *et al.,* 1980).

Table 3.4: Watson Formula (Watson *et al*., 1980)

Gender	**Calculation**
Male	2.447 - (0.09156 x age) + (0.1074 x height) + (0.3362 x weight)
Female	-2.097 + (0.1069 x height) + (0.2466 x weight)

The weekly Kt/V is described in formula described below (Moosa *et al.,* 2006).

Total creatinine clearance = Peritoneal creatinine clearance + Renal creatinine clearance

Peritoneal clearance = $\frac{\text{Creatinine level in the 24h dialysate}}{\text{Serum Creatinine}}$

Weekly creatinine clearance = Creatinine clearance x 7

The renal component was calculated as the average of urea clearance and creatinine clearance in the urine. The value of the total clearance was corrected for 1.73m^2 body surface area (BSA), by using the formula of Du Bois (DuBois & DuBois, 1996). This formula is described below (DuBois & DuBois, 1996).

$$BSA\ (m^2) = 0.007184 \times W^{0.425} \times H^{0.725}$$

Where BSA = body surface area (m^2), W = weight (kg), H = height (m)

The target goals for the Kt/V or adequate dialysis are at least 2.0 and 70L/week/1.73 m^2 respectively (Moosa *et al.,* 2006). The adequacy of dialysis was classified as indicated in Table 3.5.

Table 3.5: Adequacy of dialysis

Adequacy of dialysis	Inadequate dialysis	Adequate dialysis
Kt/V	≤2.0	≥2.0
Creatinine clearance	≤ 70	≥ 70

3.2.4 Techniques

Data collection sheets were used to streamline the data collection process in Frere Hospital. The questions were specific to the study's aims and objectives. The researcher completed the data collection forms at each monthly assessment of all participants.

3.2.4.1 Socio-demographic and medical information

The researcher obtained this information from the participant's medical file and from interviewing the participant during the participant's monthly follow up session in the renal unit. This information was captured in Appendix 1.

3.2.4.2 Medical history

The researcher obtained this information from the participant's medical file and from interviewing the participant during the participant's monthly follow up session in the renal unit. This information was captured in Appendix 1.

3.2.4.3 CAPD regimen

This information was found in the participant's file. This information was captured in Appendix 1.

3.2.4.4 Nutritional status of participants receiving CAPD

i. Anthropometry measurements

The participant's edema-free body weight (measured in kilograms) and height (measured in meters) was calculated by using the Rigel Medical scale in a private separate room in the renal unit at Frere Hospital. This information was captured in Appendix 2. This scale was previously used in the renal unit. The participant's actual body weight was calculated after the complete drainage of the last dialysis exchange. The researcher estimated the degree of fluid overload (if any) in patients and the necessary weight corrections were made.

The participant's MUAC was measured on their dominant arm, by measuring the upper arm circumference at the midpoint between the lateral projection of the acromion process of the scapula and the inferior margin of the olecranon process of the ulna (Mitch & Ikizler, 2010). The AMA was calculated using the Frisancho formula (Frisancho, 1981), using a metric tape measure. The participant's TSF was measured in the dominant arm, on the posterior part of the arm, over the triceps muscle and at the midpoint of the arm, at the same point where MUAC was measured.This measurement was repeated three times to the closest 0.1mm, using *John Bull, British Indications* skin callipers previously used in Frere Hospital. The researcher was trained and standardized in taking these various measurements. The calliper was calibrated before measuring each skin fold.

ii. SGA nutrition assessment tool

The SGA nutrition assessment tool was previously not used as the standard care of the participants. It was therefore a new practice performed by the researcher alone, with the nurse confirming these results and readings.

Although it is advised that investigators performing the SGA nutrition assessment tool be formally trained through the NKF training program (Steiber *et al.,* 2004), and the researcher did not formally undergo this program, she did receive similar training on this method through her BSc.Dietetics degree in South Africa. These measurements were done in a private separate room in the renal unit at Frere Hospital and captured in Appendix 3. The SGA nutrition assessment tool consists of two sections, the first section evaluates the participant's history and the second section consists of a physical examination. The scores of both sections were added together and a final score was given.

iii. Biochemical measures

All biochemical data obtained from participants' forms were part of routine nutritional and medical care of patients at Frere Hospital. This information was captured in Appendix 4. Previously, this was the only assessment tool used in the nutritional and medical care plan of the participants. Blood samples were taken by the CAPD nurses during the participants' routine monthly visits to the renal unit. Three vials of blood were taken from each participant, as part of their monthly assessments. Each vial contained 5ml of blood. The samples were transported to and stored and measured according to standard prescribed laboratory procedures specific for each biochemical marker by the NHLS, Clinical Pathology Sanas at Frere Hospital.

iv. Dietary intake

The dietary intake was assessed using three 24-hour recalls, which increases the validity of the trial (Nelson & Bingham, 1997, Thompson & Byers, 1994). This information was captured in Appendix 5. An average of three consecutive days of 24-hour recalls was captured and evaluated to ensure valid results at baseline and during the two months of the intervention period of the trial. Dietary intake data was not previously used as standard of care in the patients at Frere Hospital, and therefore this was a new practice done in the participants for this trial. The researcher used the SA Medical Research Council (MRC) *Food Flash Cards* and *Food Photo Manual* in establishing correct portion sizes and cooking methods (Steyn & Senekal, 2004). The SA MRC Food Quantities Manual (Langenhoven *et al*., 1991) to assist with the conversion of food intake reported in household measures. The 24-hour recall records were analysed by the researcher, with the aid of Food Finder 3 for Windows, which is based on the MRC Food Composition Database (FoodFinder 3, 2012: online). This computer diet-analysis program based on typical foods in SA, as well as the portion sizes and cooking and preparation methods of the food items (FoodFinder 3, 2012: online).

The diet was not controlled in this trial as the investigators wanted to see the overall effect of protein supplementation, together with a normal home diet in the experimental group, and not a strictly controlled diet.

3.2.4.5 Protein supplementation

Each participant in the intervention group received a monthly supply of *Protifar,* during routine follow-up assessments in hospital, over a period of three months. This information was captured in Appendix 6 – 8. Participants were trained in the directions for use. The researcher calculated, and measured out the prescribed amount of *Protifar* powder for each individual participant according to the participants' baseline edema-free adjusted body weight and nutritional needs (0.65g/kg/day protein powder only). The *Protifar* powder was stored in individual containers, marked with the participant's folder number, amount of powder, day and date. This ensured good quality control over the amount of *Protifar* powder prescribed per participant. The participants filled out a form to document their daily intake of the protein supplement, on their own (and without help from the investigator) and gave reasons if they did not add the powder to their food for that particular day, as captured in Appendix 6 – 8. The researcher calculated the average total protein intake over the three month intervention period. The researcher subtracted any days missed from protein supplementation, from the total protein intake (a score was tallied on the data collection sheet). This enabled the researcher to assess the participant's compliance and reasons for non-compliance. This information may be used in the planning of future studies of protein supplementation in patients receiving CAPD in a South African setting.

3.2.4.6 Efficiency of dialysis

Peritoneal urea, creatinine and protein excreted were measured. This information was captured in Appendix 9. This was previously not used as standard care practice of the patients at Frere Hospital and was therefore be a new practice introduced to the participants. The researcher gathered the data for the adequacy measurements at the participants' monthly follow-ups at the renal unit.

Participants brought in their four peritoneal bags and a 24-hour urine sample (if available) from the previous day. Participants received a urine sample bottle from Frere Hospital at the visit preceding data collection. The researcher contacted each participant telephonically the preceding day to remind them to bring the urine and peritoneal dialysate samples. Five ml of dialysate was taken from each peritoneal bag after the last exchange by the peritoneal dialysis nurses and analysed at the NHLS, Clinical Pathology Sanas at Frere Hospital.

3.2.5 Validity and reliability

3.2.5.1 Validity

Validity is defined as the degree to which instruments achieve the function for which they are being used (Worthern *et al*., 1993; Mehrens & Lehman, 1987).

The aims of the trial were directly addressed through the questionnaires in order to ensure validity. The questions were based on an in-depth literature study. This trial compared the measurements to scientific and evidence-based recommendations in order to increase validity. Dietitians and doctors, who are experts in the field, were also consulted to comment on the questionnaire in order to increase the content validity.

Translation of the English questionnaires into Afrikaans and Xhosa were kept as directly as possible as not to lose the validity of questions. This was done with the help from dietitians and nutrition assistants working at Frere Hospital.

Validity was enhanced by the following steps:

i. The available CAPD solutions on the government tender were used in the CAPD Regime (Appendix 1);
ii. The usefulness and reproducibility of the SGA nutrition assessment tool has been successfully studied in the CAPD population and therefore no pilot study was performed on this tool (Enia *et al.,* 1993) (Appendix 3);
iii. Blood was collected from the participants using the same procedures currently used at Frere Hospital, and the biochemical cut-off points defined by the NHLS (used in all the Department of Health Hospitals in the Eastern Cape) was used (Appendix 4);
iv. The *MRC Food Flash Cards* and *Food Photo Manual* were used in establishing correct portion sizes and cooking methods (Steyn and Senekal, 2004). The MRC *Food Quantities Manual* (Langenhoven *et al*., 1991) assisted with the conversion of food intake reported in household measures (Appendix 5);

3.2.5.2 Reliability

Reliability is defined as the degree of consistency between two measures of the same thing (Mehrens and Lehman, 1987). The measure of how stable, dependable, trustworthy and consistent a test is in measuring the same thing every time it is used (Worthen *et al.,* 1993).

Reliability was enhanced by the following steps:

i. The adequacy of dialysis was assessed in two different ways, namely Kt/V formula and the weekly creatinine clearance. The Watson formula was used in the Kt/V formula, in which the participant's gender, age, height and weight were taken into consideration. The duBois Formula was used in the calculation of the creatinine clearance to correct the participant's body surface area (Appendix 9);

ii. The *Speaking Books Informed Consent Book* was used to obtain informed consent from illiterate participants, in which various pictures, writing, and verbal communication were used, in order to ensure that participants fully understood what was expected of them in the trial.

iii. The anthropometry measurements were taken only by the researcher, using standard practices. All measuring tools were calibrated to zero before use. The same tools were used for every measurement for every participant at each consecutive follow-up session. An average of three measurements was taken for the weight, height, MUAC and TSF. The researcher was trained and standardised in the collection of anthropometry measurements and made the necessary weight corrections for edema present in a participant (Appendix 2)

iv. Each biochemical marker was measured according to the NHLS, and if a result came back as abnormally high or abnormally low, the researcher ensured that the specific biochemical marker was measured again by means of an immediate duplicate blood sample (Appendix 4);

v. The average dietary intakes based on three 24-hour recalls was used (Appendix 5);

vi. Care was taken to ensure that questions were not ambiguous and was easy to understand in the participants' home language. All appendices were translated into Afrikaans and Xhosa;

vii. Participants were ensured that all results would be kept strictly confidential; and

viii. All protein powder to be used by the intervention group, was measured out into individual airtight containers by the researcher, according to the participant's edema-free body weight at the baseline assessment.

ix. The researcher documented the data (on Appendices 1-9) and transferred the data independently on two separate Excel files on different occasions, so that two independent Excel sheets with the data was submitted to the biostatistician, who verified the data.

3.2.6 Statistical analysis

All data was captured into *Microsoft Excel 2007* and exported to statistical software for analysis. The data analysis for this study was done using SAS software, Copyright, SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA. The statistical analysis was performed by the Department of Biostatistics of the Faculty of Health Science of the University of the Free State and data was tested for normality. Descriptive statistics were used and data were expressed as medians and percentiles for continuous data and frequencies and percentages for categorical data, for the baseline and the follow-up per group. The change from baseline to follow-up was calculated, expressed as medians, and compared between the two groups, using 95% confidence intervals. If there were fewer than six participants in a group, the p-value was calculated with the Kruscal Wallis test. A p-value <0.05 was considered significant.

3.2.7 Pilot study

Before the start of the trial, a pilot study was completed at the renal unit of Frere Hospital to test the feasibility of the trial and understandability of the questionnaires. The anthropometry, biochemical measures and 24-hour recall was piloted in the study group to streamline data collection processes and assess the flow of data collection in the renal unit.

Ten percent (n=3) of the study population was used for the pilot study. No alterations were made to the questionnaires and therefore the results obtained during the pilot study were included in the main study results.

3.2.8 Study procedure

Approval for the trial was obtained from the Ethics Committee of the Faculty of Health Sciences at the University of the Free State (ECUFS 122/2012) and the Chief Executive Officer of Frere Hospital. Before any information was collected from the participants, informed consent was obtained. Figure 3.2 represents the framework compiled for the purpose of this trial. Data was collected at monthly points during the intervention.

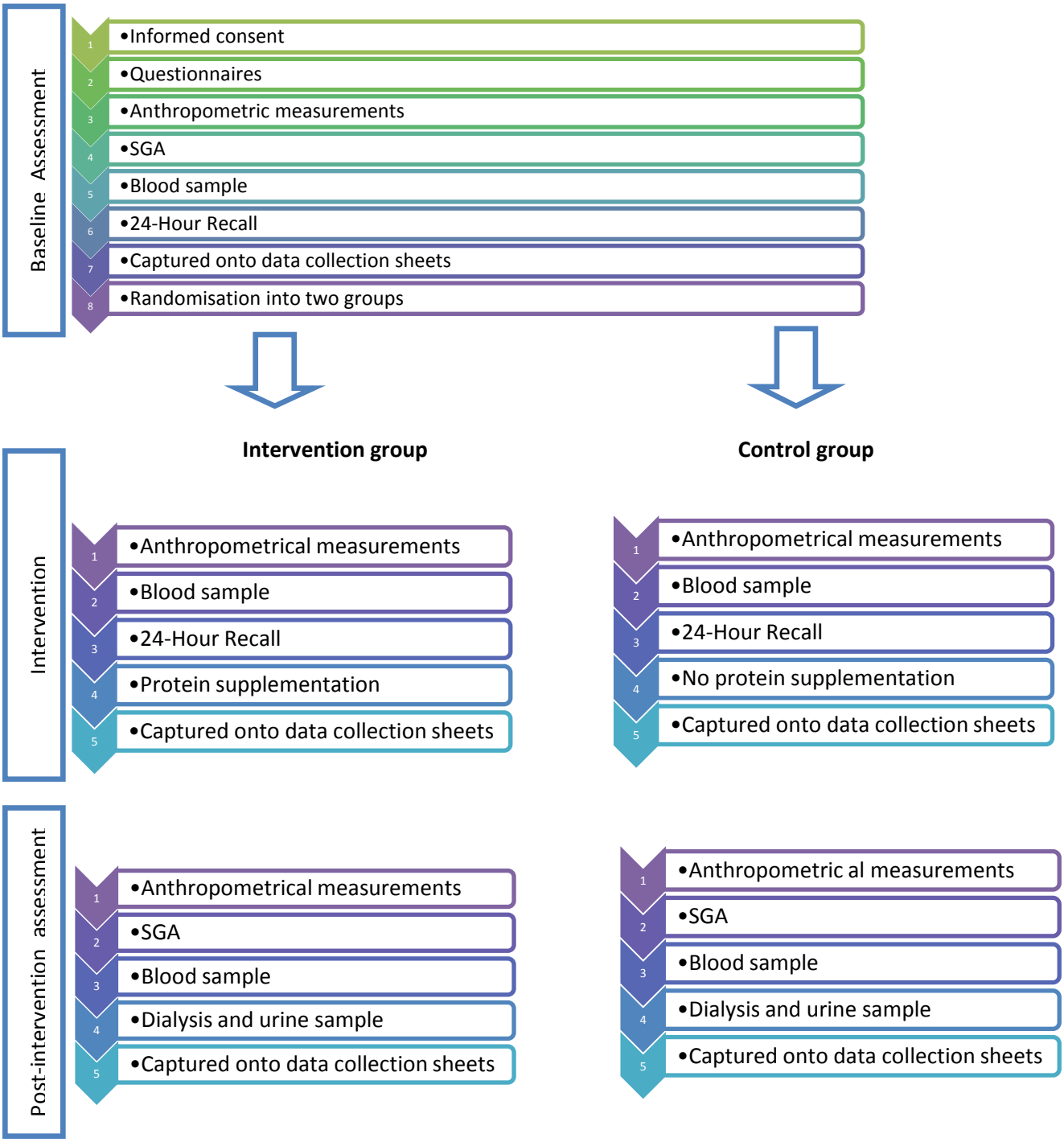

Figure 3.2: Framework to describe procedure

3.2.8.1 Health care workers

The roles and responsibilities of each health care worker are defined in Table 3.6

Table 3.6 Health Care worker roles and responsibilities

Role in trial	Responsibility
Researcher	Anthropometric measurements Completion of SGA nutrition assessment tool Collection of 24-hour recall data Distribution of protein powder Capturing data and calculating Kt/V and creatinine clearance onto data collection sheets at the end of trial
Physician Specialist at Renal Unit, Frere Hospital	Medical care of participants Scientific input and feedback on literature study, literature review, protocol, article submission
Professional nurses at Renal Unit, Frere Hospital	Collection of blood samples Collection of dialysate, urea and creatinine Assist in the translation of Xhosa speaking participants with reference to the Informed Consent and 24 hour recall

3.2.8.2 Participants

The participants in the intervention group received one month's supply of the pre-marked and individualised protein supplement. These measurements were recorded monthly onto the data collection sheets for the three month duration of the trial (Appendix 6 – 8).

Baseline assessment was repeated at the end of the trial to evaluate the participants' nutritional status and other assessments as mentioned in the baseline assessments. The researcher coded all of the questionnaires and the Department of Biostatistics at the University of the Free State analyzed the data. Figure 3.3 illustrates the flow of the data collection process.

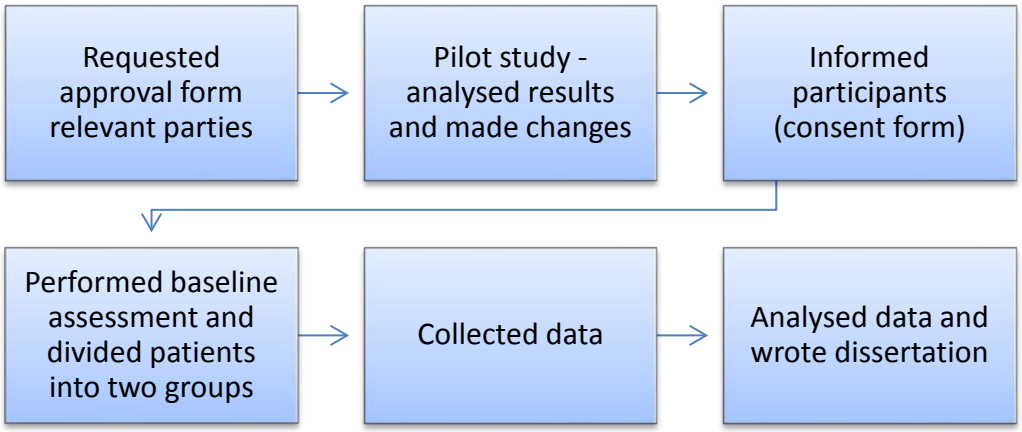

Figure 3.3: Data collection process

3.2.9 Ethical aspects

3.2.9.1 Ethical approval

Approval for the trial was obtained from the Ethics Committee of the Faculty of Health Sciences at the University of the Free State (ECUFS 122/2012) and the relevant authorities atFrere Hospital.

3.2.9.2 Informed consent

Informed consent (Appendix 10 – 12) was obtained from the participants in the pilot and the main study. The informed consent and information document (Appendix 13 – 15) was signed by all participants. Informed consent forms and information documents were available in English, Afrikaans and Xhosa. Illiterate participants were able to take part in the trial usingthe *Speaking Books Informed Consent Book*, in which various pictures, writing, and verbal communication explained informed consent to the participants. The researcher was available at the informed consent session to answer any questions that the participants might have had.

All information and data obtained from the trial was treated as confidential at all times. Participation in the trial was completely voluntary. There was no remuneration or costs to the participants. All participants in the trial received a lunch meal from Frere Hospital during the baseline and monthly assessments. The blood results taken from the participants were routine practice in the Frere Renal Unit.

3.2.9.3 Sponsorship of protein powder

The protein supplement, *Protifar,* was supplied by the Dietetics Department of Frere Hospital. No financial aid or *Protifar* powder was provided by the manufacturing company, Nutricia. The control group received the current standards of care at Frere Hospital, and was therefore not disadvantaged during the trial.

Chapter 4: Results

4.1 Introduction

At baseline the socio-demographic information, medical history, CAPD regimen and nutritional status of the study population were described and compared between the experimental and control groups. Data related to nutritional status were collected post-intervention and at monthly intervals during the course of the intervention, and compared between the experimental and control groups. Post-intervention, the changes that occurred in nutritional status within each group from baseline, were summarised, and compared between the experimental and the control groups. As the data was non-parametrically distributed, probably due to the small sample size, results for continuous data were presented as medians and percentiles. Categorical data was presented as frequencies and percentages. Comparisons by means of 95% confidence intervals (CI) for median or percentage differences, or the p-value calculated with the Kruscal Wallis test where appropriate, are indicated on the tables.

4.2 Baseline assessment

At baseline the socio-demographic information, medical history, CAPD regimen, and nutritional status were recorded, and the medians and frequencies compared between the experimental and control groups.

4.2.1 Socio-demographic information

The median age of participants at baseline was 39.8 years in the experimental group (25 to 54 years old) and 37.2 years in the control group (24 to 51 years old). Most of the participants in both groups were female (9 participants in the experimental group and 10 participants in the control group) , and Black (10 participants in the experimental group and 10 participants in the control group). Only a third of participants in both groups lived closer than 50 km from the dialysis unit, while 15% in the experimental group and 25% in the control group lived more than 201 km away. There was no significant difference between the two groups with regard to how many participants lived more than 50 km away from Frere Hospital (95% CI for the percentage difference [-30.6%; 35.6%]). The median number of people living with the participant in both groups was three people (95% CI for the median difference [-1; 2]). Most of the participants in both groups were unemployed (4 participants in the experimental group and none in the control group) or relied on a grant as source of income (7 participants in the experimental group and 10 participants in the control group).

There were no significant differences between the two groups with regard to the number of participants who received grants (95% CI for the percentage difference [-56.9%; 6.8%]), but significantly more were unemployed in the control group than in the experimental group (95% CI for the percentage difference [0.5%; 57.6%]).

4.2.2 Medical history

The aetiology of the participant's renal failure, existing co-morbidities, and medication was assessed. In most of the participants - 84.6% (n=11) in the experimental group and 75% (n=9) in the control group - the cause of CRF was indicated in the participants' medical files as hypertension. Diabetes Mellitus, glomerular nephritus and tuberculosis were not recorded as the cause of CRF in any of the participants. The cause of renal failure was due to: nephrotic syndrome in on participant (7.7%) in the experimental group, systemic lupus erythematosus in one participant (8.3%) in the control group, nephrectomy in one participant (8.3%) in the control group, and nephritis in one participant (7.7%) in the experimental group.

Hypertension was the most frequent existing co-morbidity in both groups, occurring in 100% of the experimental group and 84.6% of the control group. Diabetes occurred in about a fifth of the study population (23.1% of the experimental group and 15.4% of the control group) and anemia in almost half of the study population (46.2% of the experimental group and 38.5% of the control group). Other co-morbidities included SLE (15.4% of the experimental group and 7.7% of the control group), gout (none of the experimental group and 7.7% of the control group), DVT (15.4% of the experimental group and none of the control group), nephrotic syndrome (7.7% of the experimental group and none of the control group), polycystic kidney disease (none of the experimental group and 7.7% of the control group), pulmonary edema (none of the experimental group and 7.7% of the control group) and diabetic retinopathy (none of the experimental group and 7.7% of the control group).

Most of the participants used ACE inhibitors (92.3% of the experimental group and 91.7% of the control group), anti-anaemic preparations (69.3% of the experimental group and 66.7% of the control group), calcium channel blockers (100% of the experimental group and 75% of the control group) and calcium carbonate (as antiacid) (100% of the experimental group and 91.7% of the control group), and more than half in both groups were using folic acid supplements (53.9% of the experimental group and 58.3% of the control group). There were no statistical significant differences between the two groups at baseline regarding the types or dosages of medication used.

4.2.3 CAPD regimen

The median duration that participants had been receiving CAPD at the time of the trial was five months in the experimental group (1 to 33 months) and eight months (3 to 100 months) in the control group (95% CI for the median difference [-9; 6]). Most participants were receiving a combination of 1.5% and 2.5% Dianeal solution in two litre volumes per exchange. Most participants did four daily exchanges: 84.6% (n=11) in the experimental group (mean 4 bags) and 92.3% (n=12) in the control group (mean 4 bags) (95% CI for the median difference [0; 0]). Most participants in both groups had a HD line present as well: 61.5% (n=8) in the experimental group and 76.9% (n=10) in the control group (95% CI for the median difference [0; 0]). No statistical significance was noted regarding any aspects related to CAPD regimen between the two groups at baseline (for number of daily exchanges: 95% CI for the percentage difference [-28.4%; 25.9%]; for presence of a HD line: 95% CI for the percentage difference [-44.1%; 21.6%]).

4.2.4 Nutritional status at baseline

The nutritional status, including anthropometry measurements, SGA nutrition assessment tool, biochemical measures, and dietary intakes, were recorded and compared between the experimental and control groups. These data are summarised in Tables 4.1 to 4.3.

4.2.4.1 Anthropometry measurements

The anthropometry measurements at baseline were captured and categorised in Table 4.1. The median edema-free body weight was 65.2 kg (49.0 to 94.5 kg) in the experimental group and 64.1 kg (57.8 to 96.6 kg) in the control group. Edema was present in six participants (46.2%) in the experimental group (maximum 2.5kg) and three participants (23.1%) in the control group (maximum 1.5kg) (95%CI for the percentage difference [-12.5%; 51.9%]). No statistical significantly differences were noted between the two groups at the baseline regarding any of the anthropometry measurements.

The participants' BMI (based on edema-free body weight) were classified into four categories in Table 4.1, according to recommended ranges for patients receiving CAPD (KDOQI, 2013). None of the participants were underweight; most had a normal BMI; and more than a third of participants in both groups were overweight/obese at baseline. The percentage of participants who were overweight or obese were not significant different between the two groups.

For the purpose of this trial MUAC and TSF were measured in order to calculate the AMA using the Frisancho formula (Frisancho, 1981; KDOQI, 2013). AMA is expressed in Table 4.1 in percentiles according to recommended ranges for patients receiving CAPD (Frisancho, 1981). At baseline most of the participants (69.2% in the experimental group) and more than half of the participants (54.6% in the control group) had a normal, to above average muscle mass, based on AMA. Only one participant in each group (±8%) were classified as wasted based on AMA (95% CI for percentage difference [-28.4%; 25.9%], with a further 20% to 40% having below average muscle mass in both groups. The percentage of participants who were waisted based on AMA, were not significant different between the two groups.

Table 4.1: Anthropometry of the two groups at baseline (Frisancho, 1981; KDOQI, 2013)

Variable	Experimental group (n=13)		Control group (n=13)		95% CI for the percentage difference
	n	%	n	%	
BMI [#]					
Underweight (≤18.5 kg/m^2)	0	0.0	0	0.0	
Normal (18.5-24.9 kg/m^2)	8	61.5	9	69.2	
Overweight (25.0-29.9 kg/m^2)	3	23.1	2	15.4	[-26.3% ; 39.4%]
Obese (≥ 30 kg/m^2)	2	15.4	2	15.4	
AMA [§]					
Wasted (<5th percentile)	1	7.7	1	8.3	[-28.4%; 25.9%]
Below-average (5th- 25th percentile)	3	23.1	4	33.3	
Normal (25th- 75th percentile)	7	53.8	3	25.0	
Above-average (75th- 95th percentile)	1	7.7	3	25.0	
High (>95th percentile)	1	7.7	1	8.3	

[#] Based on edema-free body weight

[§] Calculated from MUAC and TSF and representing muscle mass

4.2.4.2 SGA nutrition assessment tool

At baseline the majority of participants of both groups (61.5% (n=8) in the experimental group and 84.6% (n=11) of the control group) were classified as well-nourished based on SGA nutrition assessment tool score. Only 30.8% (n=4) of the experimental group and 16.7% (n=2) of the control group were classified as mildly/moderately malnourished, and this was not siginificant different between the groups. Only one participant (7.7%) in the experimental group was severely malnourished. The percentage of participants who were mildly/moderately malnourished (95% CI for the percentage difference [-17.0%; 44.4%]), or severely malnourished (95% CI for the percentage difference [-16.0%; 33.3%]), were not significant different between the two groups.

4.2.4.3 Biochemical measures

No statistical significance difference regarding median biochemical measures were noted between the two groups at baseline.

The biochemical measures, including albumin levels, electrolytes and protein waste products, for each group at baseline were categorised as either below normal, normal, or above normal in Table 4.2 and were compared to recommended reference ranges used by the NHLS at Frere Hospital. The CRP was not obtained in the trial due to lack of resources in the hospital. The majority of the participants (92.3% in the experimental group and 91.7% in the control group) had below normal serum albumin levels with a median value of 29g/L in both groups. Serum sodium and potassium levels seemed to be well controlled with values ranging from low to normal in both groups, while serum phosphate levels were elevated in a third of the experimental group and two thirds of the control group.

The serum concentrations of the waste products, urea and particularly creatinine, were increased and above normal range values in almost all of the participants. The median serum urea level of the experimental group was twice, and that of the control group, three times the upper limit of the normal range. The mean serum creatinine level was about eight times the upper limit of the normal range in both groups.

Table 4.2: Biochemistry of the two groups at baseline (NHLS, Frere Hospital)

Variable	Experimental group (n=13)		Control group (n=12)[#]		95% CI for the percentage difference
	n	%	n	%	
Serum albumin (g/L)					
Below normal (< 35.0)	12	92.3	11	91.7	[-25.9%; 28.4%]
Normal range (35.0 – 52.0)	1	7.7	1	8.3	
Above normal (> 52.0)	0	0	0	0	
Serum sodium (mmol/L)					
Below normal (< 135.0)	9	69.2	5	41.7	[-10.1%; 56.3%]
Normal range (135.0 – 147.0)	4	30.7	7	58.3	
Above normal (> 147.0)	0	0	0	0	
Serum potassium (mmol/L)					
Below normal (< 3.3)	3	23.1	1	8.3	[-16.1%; 42.8%]
Normal range (3.3 – 5.3)	10	76.9	11	91.7	
Above normal (> 5.3)	0	0	0	0	
Serum phosphate (mmol/L)					
Below normal (< 0.8)	2	15.4	0	0	
Normal range (0.8 – 1.4)	6	46.2	4	33.3	
Above normal (> 1.4)	5	38.5	8	66.7	[-11.3%; 42.2%]
Serum urea (mmol/L)					
Below normal (< 2.6)	0	0	0	0	
Normal range (2.6 – 7.0)	1	7.7	0	0	
Above normal (> 7.0)	12	92.3	12	100.0	[-24.3%; 22.8%]
Serum creatinine (umol/L)					
Below normal (< 64.0)	0	0	0	0	
Normal range (64.0 – 104.0)	0	0	0	0	
Above normal (> 104.0)	13	100.0	12	100.0	[-24.3%; 22.8%]
Serum cholesterol (mmol/L)[§]					
Below normal (< 5.0)	0	0	0	0	
Normal range (5.0)	0	0	2	66.7	
Above normal (> 5.0)	1	100.0	4	33.3	[-24.3%; 22.8%]

[#] Please note for this variable, there was a response of 12 participants instead of 13 participants in the control group, as the participant was not present at assessment

[§] Please note for the variable, serum cholesterol, there was a response of 1 participant in the experimental group instead of 13 and 3 participants in the control group instead of 13, as the rest of the serum cholesterol results were collected in the intervention period (Table 4 and Table 4).

4.2.4.4 Dietary intake

The participants' dietary intake was obtained, categorised and assessed according to the total energy, protein (total and HBV protein), carbohydrate and fat intakes. This data was compared to the KDOQI recommended daily intakes for patients receiving CAPD, and categorised as inadequate, adequate, or more than adequate nutrient intake (KDOQI, 2006) in Table 4.3.

No statistical significant differences regarding dietary intake were noted between the two groups at baseline, although the energy and macronutrient intakes were slightly higher in the control group than in the experimental group.

The energy and macronutrient intakes are categorised in Table 4.3 according to the KDOQI recommendations for patients receiving CAPD (KDOQI, 2006) as inadequate, adequate or more than adequate. Median energy intakes at 25.5 kCal/kg (ranging from 8.2 kCal/kg to 35.7 kCal/kg) for the experimental group and 27.5 kCal/kg (ranging from 10.6 kCal/kg to 45.3 kCal/kg) for the control group, were about 20% below the lower limit of the energy recommendation of 30 to 35 kCal/kg. More than two thirds of participants in both groups had inadequate energy intakes With the median intake of protein the experimental group at 1.0 g/kg (ranging from 0.4 g/kg to 2.2 g/kg) and that of the control group at 1.2 g/kg (ranging from 0.3 k/kg to 1.8 g/kg), more than half of the participants in both groups also had inadequate protein intakes. The intake of high biological value protein was also below recommendations in about half of the experimental group and about three quarters of the control group. Most of the participants in both groups also had inadequate intakes of carbohydrate and fat. The percentage of participants with inadequate energy, protein, HBV protein, carbohydrate or fat intakes, did not differ significantly between the two groups.

Table 4.3 Evaluation of dietary intake at baseline (KDOQI, 2006)

Variable	Experimental group (n=13)		Control group (n=12)[#]		95% CI for the percentage difference
	n	%	n	%	
Energy (kCal/kg)[§]					
Inadequate intake (< 30.0)	10	76.9	8	66.7	[-23.2%; 41.6%]
Adequate Intake (30.0 – 35.0)	2	15.4	3	25.0	
Above adequate intake (> 35.0)	1	7.7	1	8.3	
Total protein (g/kg)[¥]					
Inadequate intake (< 1.2)	7	53.9	7	58.3	[-37.8%; 30.5%]
Adequate Intake (1.2 – 1.3)	1	7.7	1	8.3	
Above adequate intake (> 1.3)	5	38.5	4	33.3	
HBV protein: animal protein (%)					
Inadequate intake (< 50.0)	7	53.9	9	75.0	[-50.6%; 15.2%]
Adequate Intake (50.0)	0	0	0	0	
Above adequate intake (> 50.0)	6	46.2	3	25.0	
Carbohydrate (% of TE)					
Inadequate intake (< 50.0)	6	46.2	7	58.3	[-44.2%; 24.0%]
Adequate Intake (50.0 – 60.0)	4	30.8	4	33.3	
Above adequate intake (> 60)	3	23.1	1	8.3	
Fat (% of TE)					
Inadequate intake (< 25.0)	8	61.5	7	58.3	[-31.1%; 36.8%]
Adequate Intake (25.0 – 35.0)	3	23.1	4	33.3	
Above adequate intake (> 35.0)	2	15.4	1	8.3	

[#] Please note for this variable, there was a response of 12 participants instead of 13 participants in the control group, as the participant was not present at assessment

[§] KDOQI guidelines are expressed as calories, while South African institutions use kilojoules as a measurement of dietary energy intake

[¥] Based on edema-free body weight and the total protein intake excludes the *Protifar* powder (protein supplement), which was supplemented at 0.65g/kg (using ABW) in the experimental group

4.3 Intervention: nutritional status after one, two and three months

During the intervention, nutritional status, which included anthropometry, SGA nutrition assessment tool, and biochemistry were recorded at the end of the first, second and third months. Dietary intakes were recorded after the first and the second months. These data were summarised and compared between the experimental and control groups (Tables 4.4 – 4.10).

4.3.1 Anthropometry measurements

The comparison between categories of anthropometrical measurements for the two groups is captured in Table 4.4. No statistically significant difference were found between the groups with regard to the prevalence of overweight/obesity based on BMI; or with regard to wasting, based on AMA measurement any of the data collection times.

Table 4.4: Difference in anthropometry of the two groups after one, two and three months (Frisancho, 1981; KDOQI, 2013)

Variable	Experimental group (n=13)		Control group (n=12)[#]		95% CI for the percentage difference
	n	%	n	%	
Month one					
BMI [§]					
Underweight (≤18.5 kg/m^2)	0	0	0	0	
Normal (18.5-24.9 kg/m^2)	7	53.9	7	58.3	
Overweight (25.0-29.9 kg/m^2)	4	30.1	3	25.0	[-30.5% ; 37.8%]
Obese (≥ 30 kg/m^2)	2	15.4	2	16.7	
AMA [¥]					
Wasted (<5th percentile)	0	0	1	8.3	[-35.4%; 15.5%]
Below-average (5th- 25th percentile)	4	30.1	2	16.7	
Normal (25th- 75th percentile)	7	53.9	5	41.7	
Above-average (75th- 95th percentile)	2	15.4	2	16.7	
High (>95th percentile)	0	0	2	16.7	
Month two					
BMI [§]					
Underweight (≤18.5 kg/m^2)	0	0	0	0	
Normal (18.5-24.9 kg/m^2)	8	61.5	7	58.3	
Overweight (25.0-29.9 kg/m^2)	3	23.1	3	25.0	[-36.8% ; 31.1%]
Obese (≥ 30 kg/m^2)	2	15.4	2	16.7	
AMA [¥]					
Wasted (<5th percentile)	1	7.7	1	8.3	[-28.4%; 25.9%]
Below-average (5th- 25th percentile)	2	15.4	2	16.7	
Normal (25th- 75th percentile)	7	53.8	6	50.0	
Above-average (75th- 95th percentile)	3	23.1	2	16.7	
High (>95th percentile)	0	0	1	8.3	
Month three					
BMI [§]					
Underweight (≤18.5 kg/m^2)	0	0	1	8.3	
Normal (18.5-24.9 kg/m^2)	8	61.5	7	58.3	
Overweight (25.0-29.9 kg/m^2)	4	30.8	2	16.7	[-29.4% ; 37.7%]
Obese (≥ 30 kg/m^2)	1	7.7	2	16.7	
AMA [¥]					
Wasted (<5th percentile)	1	7.7	2	16.7	[-37.8%; 19.3%]
Below-average (5th- 25th percentile)	0	0	1	8.3	
Normal (25th- 75th percentile)	7	53.8	5	41.7	
Above-average (75th- 95th percentile)	5	38.5	3	25.0	
High (>95th percentile)	0	0	1	8.3	

[#] Please note for this variable, there was a response of 12 participants instead of 13 participants in the control group, as the one participant died before the intervention started

[§] Based on edema-free body weight ; [¥] Calculated from MUAC and TSF and representing muscle mass

No difference in the presence of edema was documented after the first and second months, but after the third month edema was significantly more prevalent in the control group: 50% of participants had edema (n=6) versus the experimental group: 7.7% had edema (n=1)(95% CI for the percentage difference[-67.7%; -6.8%]).

4.3.2 Biochemical measures

The biochemical measures are compared to recommended reference ranges, used by the NHLS at Frere Hospital, after month one, two and three in Tables 4.5, 4.6 and 4.7.. After the second month serum potassium (95% CI for the percentage difference [22.8%; 80.2%])and after the third month serum sodium (95% CI for the percentage difference [6.5%; 64.5%], were significantly higher in the control than in the experimental group.

Table 4.5: Comparison of the biochemistry of the two groups after one month (NHLS, Frere Hospital)

Variable	Experimental group (n=13)		Control group (n=12)[#]		95% CI for the median difference
	n	%	n	%	
Serum albumin (mmol/L)					
Below normal (< 35.0)	10	76.9	10	83.3	[-36.1% ; 25.4%]
Normal range (35.0 – 52.0)	3	23.1	2	16.7	
Above normal (> 52.0)	0	0	0	0	
Serum sodium (mmol/L)					
Below normal (< 135.0)	4	30.8	4	33.3	[-35.6% ; 30.6%]
Normal range (135.0 – 147.0)	9	69.2	8	66.7	
Above normal (> 147.0)	0	0	0	0	
Serum potassium (mmol/L)					
Below normal (< 3.3)	3	23.1	2	16.7	[-25.4% ; 36.1%]
Normal range (3.3 – 5.3)	9	69.2	10	83.3	
Above normal (> 5.3)	1	7.7	0	0	
Serum phosphate (mmol/L)					
Below normal (< 0.8)	5	38.5	2	16.7	
Normal range (0.8 – 1.4)	8	61.5	10	83.3	
Above normal (> 1.4)	0	0	0	0	[-50.4% ; 13.2%]
Serum urea (mmol/L)					
Below normal (< 2.6)	0	0	0	0	
Normal range (2.6 – 7.0)	0	0	0	0	
Above normal (> 7.0)	13	100.0	12	100.0	
Serum creatinine (mmol/L)					
Below normal (< 64.0)	0	0	0	0	
Normal range (64.0 – 104.0)	0	0	0	0	
Above normal (> 104.0)	13	100.0	12	100.0	
Serum cholesterol (mmol/L)[§]					
Below normal (< 5.0)	5	55.6	5	71.4	
Normal range (5.0)	3	33.3	1	14.3	
Above normal (> 5.0)	1	11.1	1	14.3	[-41.3% ; 31.3%]

[#] Please note for this variable, there was a response of 12 participants instead of 13 participants in the control group, as the participant was not present at assessment

[§] Please note for the variable, serum cholesterol, there was a response of 9 participants in the experimental group instead of 13 and 7 participants in the control group instead of 13, as the rest of the serum cholesterol results were collected in the intervention period (Table 4.2 and Table 4.6).

Table 4.6: Comparison of the biochemistry of the two groups after two months (NHLS, Frere Hospital)

Variable	Experimental group (n=13)		Control group (n=12)[#]		95% CI for the percentage difference
	n	%	n	%	
Serum albumin (mmol/L)					
Below normal (< 35.0)	11	84.6	10	83.3	[-28.1% ; 31.5%]
Normal range (35.0 – 52.0)	2	15.4	2	16.7	
Above normal (> 52.0)	0	0	0	0	
Serum sodium (mmol/L)					
Below normal (< 135.0)	4	30.8	2	16.7	[-19.3% ; 43.5%]
Normal range (135.0 – 147.0)	9	69.2	10	83.3	
Above normal (> 147.0)	0	0	0	0	
Serum potassium (mmol/L)					
Below normal (< 3.3)	9	69.2	1	8.3	[22.8% ; 80.2%]*
Normal range (3.3 – 5.3)	4	30.8	10	83.3	
Above normal (> 5.3)	0	0	1	8.3	
Serum phosphate (mmol/L)					
Below normal (< 0.8)	2	16.7	1	8.3	
Normal range (0.8 – 1.4)	5	41.7	4	33.3	
Above normal (> 1.4)	5	41.7	7	58.3	[-48.3% ; 20.6%]
Serum urea (mmol/L)					
Below normal (< 2.6)	0	0	0	0	
Normal range (2.6 – 7.0)	0	0	0	0	
Above normal (> 7.0)	13	100.0	12	100.0	
Serum creatinine (mmol/L)					
Below normal (< 64.0)	0	0	0	0	
Normal range (64.0 – 104.0)	0	0	0	0	
Above normal (> 104.0)	13	100.0	12	100.0	
Serum cholesterol (mmol/L)[¥]					
Below normal (< 5.0)	2	66.7	1	50.0	
Normal range (5.0)	1	33.3	0	0	
Above normal (> 5.0)	0	0	1	50.0	[-90.5% ; 19.3%]

*Indicates a statistical significant difference between the two groups

[#] Please note for this variable, there was a response of 12 participants instead of 13 participants in the control group, as the participant was not present at assessment

[¥] Please note for this variable, there was a response of 3 participants in the experimental group instead of 13 and 2 participants in the control group instead of 13 during month two, as the rest of the serum cholesterol results were collected in the baseline and month one of intervention period (Table 4.2 and Table 4.5).

Table 4.7: Comparison of the biochemistry of the two groups after three months (NHLS, Frere Hospital)

Variable	Experimental group (n=13)		Control group (n=12)#		95% CI for the percentage difference
	n	%	n	%	
Serum albumin (mmol/L)§					
Below normal (< 35.0)	7	58.3	10	90.9	[-60.0% ; 3.8%]
Normal range (35.0 – 52.0)	5	41.7	1	9.1	
Above normal (> 52.0)	0	0	0	0	
Serum sodium (mmol/L)					
Below normal (< 135.0)	5	38.5	0	0	[6.5% ; 64.5%]*
Normal range (135.0 – 147.0)	8	61.5	12	100.0	
Above normal (> 147.0)	0	0	0	0	
Serum potassium (mmol/L)					
Below normal (< 3.3)	7	53.9	2	16.7	[-0.3% ; 63.1%]
Normal range (3.3 – 5.3)	6	46.2	10	83.3	
Above normal (> 5.3)	0	0	0	0	
Serum phosphate (mmol/L)§					
Below normal (< 0.8)	1	8.3	1	9.1	
Normal range (0.8 – 1.4)	6	50.0	6	54.6	
Above normal (> 1.4)	5	41.7	4	36.4	[-30.7% ; 39.1%]
Serum urea (mmol/L)					
Below normal (< 2.6)	0	0	0	0	
Normal range (2.6 – 7.0)	0	0	0	0	
Above normal (> 7.0)	13	100.0	12	100.0	
Serum creatinine (mmol/L)					
Below normal (< 64.0)	0	0	0	0	
Normal range (64.0 – 104.0)	0	0	0	0	
Above normal (> 104.0)	13	100.0	12	100.0	

*Indicates a statistical difference between the two groups

Please note for this variable, there was a response of 12 participants instead of 13 participants in the control group, as the one participant died before the intervention started

§ Please note for these variables, there was a response of 12 participants in the experimental group instead of 13 and 11 participants in the control group instead of 13, as these blood results went missing and was not taken again due to time constraints/limited resources

4.3.3. Dietary intake

The comparison of mean energy and macronutrient intakes of participants, with the 95% CI for the median difference between the groups are summarised in Table 4.8 while Table 4.9 and Table 4.10 summarises the dietary data categorically. At month one there was no statistical significant difference between the two groups regarding dietary intake expressed as either categorical or continuous data, although fat and energy intakes were significantly higher in the control than in the experimental group at month two. Continuous data showed a tendency for the experimental group to have lower intakes of total energy, total protein, animal protein, carbohydrate and fat.

Table 4.8: Comparison of the median energy and macronutrient intakes between the two groups after one and two months

Variable	Month	Experimental group (n=13)		Control group (n=12)[#]		95% CI for the median difference
		Median	Minimum; maximum	Median	Minimum; maximum	
Energy (kJ)[§]	One	6726.0	2177.00; 10466.0	6413.0	3728.0; 8402.0	[-1421.0; 2047.0]
	Two	6637.0	1519.0; 8237.0	7478.5	3742.0; 9964.0	[-3558.0; -106.0]*
Energy (kCal/kg)[¥]	One	22.2	5.8; 50.4	21.2	14.4; 29.8	[-4.0; 9.2]
	Two	18.8	7.2; 29.4	32.0	16.7; 36.4	[-16.6; -2.6]*
Carbohydrates (g)	One	185.3	66.3; 410.0	183.8	116.6; 320.9	[-66.8; 94.2]
	Two	210.0	46.6; 301.9	237.8	61.8; 328.0	[-127.2; 17.8]
Total protein (g)[₮]	One	60.4	24.1; 128.7	51.0	38.7; 89.6	[-11.5; 22.4]
	Two	52.8	9.3; 127.3	62.9	43.1; 110.4	[-32.7; 8.3]
Protein (g/kg)[3]	One	0.9	0.3; 2.6	0.8	0.6; 1.1	[-0.1; 0.3]
	Two	0.8	0.2; 2.0	1.0	0.6; 1.7	[-0.6; 0.1]
HPV protein: Animal protein (g)	One	39.0	2.9; 95.2	35.8	12.8; 70.2	[-15.0; 18.4]
	Two	28.8	0; 100.4	36.7	11.0; 82.8	[-24.9; 17.6]
Plant protein (g)	One	21.5	9.7; 51.0	23.8	5.4; 45.4	[-8.8; 13.0]
	Two	19.7	8.4; 38.4	29.5	8.8; 44.5	[-18.1; 0.3]
Fat (g)	One	28.8	12.2; 85.2	39.1	19.5; 73.5	[-21.5; 8.7]
	Two	33.6	7.7; 52.5	46.1	11.9; 116.4	[-36.5; -2.1]*

*Indicates a statistical difference between the two groups

[#] Please note for this variable, there was a response of 12 participants instead of 13 participants in the control group, as the one participant died before the intervention started

[§] KDOQI guidelines are expressed as calories, while South African institutions use kilojoules as a measurement of dietary energy intake

[¥] Based on edema-free body weight

[₮] Total protein intake excludes the *Protifar* powder (protein supplement), which was supplemented at 0.65g/kg (using ABW) in the experimental group as this table just indicates dietary intake without supplementation

The dietary intakes are expressed in Table 4.9 and Table 4.10 and categorised as inadequate, adequate or more than adequate nutrient intake as compared to the KDOQI recommended daily intakes for patients receiving CAPD (KDOQI, 2006).

The total energy and protein intake in the experimental group excluded the protein powder supplementation. Median energy intakes at 22.2 kCal/kg (ranging from 5.8 kCal/kg – 50.4 kCal/kg) for the experimental group and 21.2 kCal/kg (ranging from 14.4 kCal/kg – 29.8 kCal/kg) for the control group, were mostly below the lower limit of the energy recommendation of 30 – 35 kcal/kg for month one of the intervention (Table 4.8).

Median energy intakes at 18.8 kCal/kg (ranging from 7.2 kCal/kg – 29.4 kCal/kg) for the experimental group and 32.0 kCal/kg (ranging from 16.7 kCal/kg – 36.4 kCal/kg) for the control group, were mostly below the lower limit of the energy recommendation of 30 – 35 kcal/kg for month two of the intervention (Table 4.8). A statistical difference for the energy intake between the two groups was found after month two of the intervention (Table 4.10).

The median intake of protein in the experimental group was 0.9 g/kg (ranging from 0.3 g/kg – 2.6 g/kg) and that of the control group was 0.8 g/kg (ranging from 0.6 g/kg – 1.1 g/kg) (Table 4.8), most of the participants in both groups also had inadequate protein intakes for month one of the intervention (Table 4.9). The intake of high biological value protein was also below recommendations in about two thirds of the experimental group and about three quarters of the control group at one month of the intervention (Table 4.9). With the mean intake of protein the experimental group at 0.8 g/kg (ranging from 0.2 g/kg – 2.0 g/kg) and that of the control group at 1.0 g/kg (ranging from 0.6 g/kg – 1.7 g/kg) (Table 4.8), most of the participants in the experimental group and two thirds of the participants in the control group also had inadequate protein intakes in month two of the intervention (Table 4.10). The intake of high biological value protein was also below recommendations in about three quarters of the intervention and control groups (Table 4.10). Most of the participants in both groups also had inadequate intakes of carbohydrate.

Median fat intakes at 28.8% of TE for the experimental group and 39.1 % of TE for the control group, were mostly below the lower limit for fat recommendation, which is 25 – 35% of TE, for month one of the intervention (Table 4.8). Median fat intakes were 33.6% of TE for the experimental group and 46.1% of TE for the control group for month two of the intervention (Table 4.8). The intake of dietary fat was below recommendations in more than three quarters of the experimental group and in half of the control group for month two of the intervention (Table 4.10). A statistical difference for the fat intake between the two groups was noted during month two of the intervention (Table 4.8).

Table 4.9 Comparison of the categories of energy and macronutrient intakes between the two groups after one month (KDOQI, 2006)

Variable	Experimental group (n=13)		Control group (n=12)[#]		95% CI for the percentage difference
	n	%	n	%	
Energy (kCal/kg)[§]					
Inadequate intake (< 30.0)	9	69.2	12	100	[57.6%; -0.5%]*
Adequate Intake (30.0 – 35.0)	3	23.1	0	0	
Above adequate intake (> 35.0)	1	7.7	0	0	
Total protein (g/kg)[¥]					
Inadequate intake (< 1.2)	10	76.9	12	100	[-50.3%; 5.4%]
Adequate Intake (1.2 – 1.3)	0	0	0	0	
Above adequate intake (> 1.3)	3	23.1	0	0	
HBV protein: animal protein (%)					
Inadequate intake (< 50.0)	9	69.2	9	75.0	[-37.1%; 27.8%]
Adequate Intake (50.0)	0	0.0	1	8.3	
Above adequate intake (> 50.0)	4	30.8	2	16.7	
Carbohydrate (% of TE)					
Inadequate intake (< 50.0)	1	7.7	2	16.7	[-37.8%; 19.3%]
Adequate Intake (50.0 – 60.0)	9	69.2	7	58.3	
Above adequate intake (> 60)	3	23.1	3	25.0	
Fat (% of TE)					
Inadequate intake (< 25.0)	9	69.2	5	41.7	[-10.1%; 56.3%]
Adequate Intake (25.0 – 35.0)	3	23.1	5	41.7	
Above adequate intake (> 35.0)	1	7.7	2	16.7	

*Indicates a statistical difference between the two groups

[#] Please note for this variable, there was a response of 12 participants instead of 13 participants in the control group, as the one participant died before the intervention started

[§] KDOQI guidelines are expressed as calories, while South African institutions use kilojoules as a measurement of dietary energy intake

[¥] Based on edema-free body weight and the total protein intake excludes the *Protifar* powder (protein supplement), which was supplemented at 0.65g/kg (using ABW) in the experimental group as this table just indicates dietary intake without supplementation

Table 4.10 Comparison of the categories of energy and macronutrient intakes between the two groups after two months (KDOQI, 2006)

Variable	Experimental group (n=13)		Control group (n=12)[#]		95% CI for the percentage difference
	n	%	n	%	
Energy (kCal/kg)[§]					
Inadequate intake (< 30.0)	13	100.0	4	36.4	[27.3% ; 84.8%]*
Adequate Intake (30.0 – 35.0)	0	0	5	45.5	
Above adequate intake (> 35.0)	0	0	2	18.2	
Total protein (g/kg)[¥]					
Inadequate intake (< 1.2)	11	84.6	8	66.7	[-15.2% ; 47.7%]
Adequate Intake (1.2 – 1.3)	0	0	1	8.3	
Above adequate intake (> 1.3)	2	15.4	3	25.0	
HBV protein: animal protein (%)					
Inadequate intake (< 50.0)	10	76.9	9	75.0	[-29.7% ; 33.8%]
Adequate Intake (50.0)	0	0	0	0	
Above adequate intake (> 50.0)	3	23.1	3	25.0	
Carbohydrate (% of TE)					
Inadequate intake (< 50.0)	3	23.1	4	33.3	[-41.6% ; 23.2%]
Adequate Intake (50.0 – 60.0)	5	38.5	5	41.7	
Above adequate intake (> 60)	5	38.5	3	25.0	
Fat (% of TE)					
Inadequate intake (< 25.0)	11	84.6	6	50.0	[-1.8% ; 61.6%]
Adequate Intake (25.0 – 35.0)	1	7.7	3	25.0	
Above adequate intake (> 35.0)	1	7.7	3	25.0	

* Indicates a statistical difference between the two groups

Please note for this variable, there was a response of 12 participants instead of 13 participants in the control group, as the one participant died before the intervention started

§ KDOQI guidelines are expressed as calories, while South African institutions use kilojoules as a measurement of dietary energy intake

¥ Based on edema-free body weight and the total protein intake excludes the *Protifar* powder (protein supplement), which was supplemented at 0.65g/kg (using ABW) in the experimental group as this table just indicates dietary intake without supplementation

4.3.4 Compliance to protein supplementation (experimental group only)

The compliance to protein powder was generally good. The best compliance was recorded for the third month, while the worst compliance, was recorded for the second month. The compliance rate after month one was 88.9%, 82.4% after month two and 90.5% after month three.

Reasons for missed intake of powder included that the participants were “only able to tolerate half a bag of protein powder given”; “were sick” or “felt physically too cold to ingest the protein powder”; “generally forgot to include the protein powder into his/her meal plan”; “were out of town” or “in hospital”; or “were fluid overloaded”. The 95% CI for the median difference for paired data: powder intake [-5; 3] and missed powder intake [-4; 2]).

4.4 Post-intervention assessment and comparison with baseline

At the end of the intervention, nutritional status, which included anthropometry, SGA nutrition assessment tool, biochemistry, were recorded; the changes within each group from baseline were calculated; and these changes from baseline were compared between the experimental and control groups (Tables 4.27 to 4.37). The adequacy of dialysis was also assessed, interpreted and compared between the groups at this point (Table 3.27).

4.4.1 Anthropometry measurements

Edema was present in five participants (38.5%) in the experimental group (maximum 2.0 kg) and five participants (45.5%) in the control group (maximum 2.0 kg) at this point.

The participants’ BMI (based on edema-free body weight) categorised according to reference ranges, are summarised in Table 4.11 (KDIGO, 2013). There was no a statistically significant difference between the groups with regard to the prevalence of overweight/obesity (95% CI for the percentage difference [-40.7%; 18.3%]).

The AMA expressed as percentiles based on recommended ranges for patients receiving CAPD (Frisancho, 1981; KDIGO, 2013) are summarised in Table 4.11 AMA measurements tended to be lower in the control group than in the experimental group, but this was not statistically significant (95% CI for the percentage difference [-40.7%; 18.3%]). The prevalence of wasting based on AMA, was also not statistically significantly different between the groups [(95% CI for the percentage difference [-37.7%; 14.9%].

Table 4.11: Comparison of the changes in categories of anthropometry between the two groups from baseline to post-intervention (Frisancho, 1981; KDIGO, 2013)

Variable	Baseline				Post-intervention				95% CI for the percentage difference
	Experimental group (n=13)		Control group (n=13)		Experimental group (n=13)#		Control group (n=11)#		
BMI§									
Underweight (≤18.5 kg/m²)	0	0.0	0	0.0	0	0.0	1	9.1	
Normal (18.5-24.9 kg/m²)	8	61.5	9	69.2	6	46.2	6	54.5	
Overweight (25.0-29.9 kg/m²)	3	23.1	2	15.4	6	46.2	2	18.2	[-40.7%; 18.3%]
Obese (≥ 30 kg/m²)	2	15.4	2	15.4	1	7.7	2	18.2	
AMA¥									
Wasted (<5th percentile)	1	7.7	1	8.3	0	0.0	1	9.1	[-20.0% ; 48.7%]
Below-average (5th- 25th percentile)	3	23.1	4	33.3	3	23.1	3	27.3	
Normal (25th- 75th percentile)	7	53.8	3	25.0	4	30.8	4	36.4	
Above-average (75th- 95th percentile)	1	7.7	3	25.0	6	46.2	2	18.2	
High muscle mass (>95th percentile)	1	7.7	1	8.3	0	0.0	1	9.1	

Please note for the following variable, there was a response of 11 participants in the control group instead of 13, as one participant did not come to the investigator for anthropometry measurements (transport issues) and the one patient died before the intervention

§Based on edema-free body weight

¥ Calculated from MUAC and TSF and representing muscle mass

The median of the changes in anthropometry measurements from baseline to post-intervention, between the two groups, were compared with the 95% CI for the median differences, in Table 4.12. No significant differences were found between the two groups.

Table 4.12: Comparison of the changes in median anthropometry within the two groups from baseline to post-intervention

Variable	Experimental group (n=13)		Control group (n=11)[#]		95% CI for the median difference
	Median	Minimum; maximum	Median	Minimum; maximum	
Edema (kg)	0	-1.5; 2.5	0	-2.0; 0.5	[0 ; 1.0]
Dry weight (kg)	-1.1	-6.5; 2.5	1.0	-4.9; 4.3	[-3.8; 1.0]
BMI (kg/m^2)[§]	0.2	-2.3; 1.4	0.4	-1.7; 1.6	[-1.5; 0.5]
AMA (cm^2)[¥]	-5.6	-13.2; 19.9	-0.5	-8.6; 30.3	[-10.6; 0.5]

[#] Please note for the following variable, there was a response of 11 participants in the control group instead of 13, as one participant did not come to the investigator for anthropometry measurements (transport issues) and the one patient died before the intervention

[§] Based on edema-free body weight

[¥] Calculated from MUAC and TSF and representing muscle mass

4.4.2 SGA nutrition assessment tool

Post-intervention, the majority of participants in both groups - 91.7% (n=12) in the experimental group and 80% (n=8) in the control group) were classified as well nourished. Only one participant (7.7%) in the experimental group and two participants (20%) in the control group were classified as mildly/moderately malnourished. None of the participants were classified as severely malnourished. When comparing the changes in SGA nutrition assessment tool category from baseline assessment to post-intervention between the two groups (Table 4.13), there was a tendency for the experimental group to obtain a better SGA nutrition assessment tool score, although this was not statistically significant.

Table 4.13: Comparison of the change in SGA nutrition assessment tool category between the two groups from baseline to post-intervention

SGA nutrition assessment tool Score	Baseline				Post-intervention				95% CI for the percentage difference
	Experimental group (n=13)		Control group (n=13)		Experimental group (n=13)		Control group (n=10)[#]		
	n	%	n	%	n	%	n	%	
Well nourished	8	61.5	11	84.6	12	92.3	8	80.0	[-49.3%; 17.1%]
Mild/moderately malnourished	4	30.8	2	15.4	1	7.7	2	20.0	
Severely malnourished	1	7.7	0	0	0	0	0	0	

[#] Please note for the following variable, there was a response of 10 participants in the control group instead of 13, as two participants did not come to the investigator for SGA nutrition assessment tool measurements (transport issues) and the one patient died before the intervention

4.4.3 Biochemical measures

The post-intervention biochemical measures categorised as either below normal, normal or above normal based on the recommended reference ranges used by the NHLS at Frere Hospital, are summarised in Table 4.14. The majority of the participants in both groups (75.0% in the experimental group and 87.5% in the control group) still had below normal serum albumin levels with a median value of 33.0 g/L in the experimental group and 28.5 g/L in the control group. While serum sodium and potassium levels seemed to be well controlled with values ranging between low to normal in both groups, serum phosphate levels were above normal range values in half of the experimental group and two thirds of the control group. The serum concentrations of the waste products, urea and particularly creatinine, were increased above normal range values in all of the participants. The median serum urea level of the experimental and control groups were three times the upper limit of the normal range. The mean serum creatinine level was about eight times the upper limit of the normal range in the experimental group and ten times the upper limit of the normal range in the control group. No statistically significant differences were however apparent between the two groups.

Table 4.14: Comparison of the biochemical categories between the two groups post-intervention (NHLS, Frere Hospital)

Variable	Experimental group (n=12)[#]		Control group (n=11)[#]		95% CI for the percentage difference
	n	%	n	%	
Serum albumin (g/L)[§]					
Below normal (< 35.0)	9	75.0	7	87.5	[-42.5%; 25.7%]
Normal range (35.0 – 52.0)	3	25.0	1	12.5	
Above normal (>52.0)	0	0	0	0	
Serum sodium (mmol/L)					
Below normal (< 135.0)	4	33.3	2	18.2	[-20.2%; 45.7%]
Normal range (135.0 – 147.0)	8	66.6	9	81.8	
Above normal (> 147.0)	0	0.0	0	0	
Serum potassium (mmol/L)					
Below normal (< 3.3)	2	16.7	2	18.2	[-33.4%; 29.5%]
Normal range (3.3 – 5.3)	10	83.3	8	72.7	
Above normal (> 5.3)	0	0	1	9.1	
Serum phosphate (mmol/L)					
Below normal (< 0.8)	1	8.3	1	9.1	
Normal range (0.8 – 1.4)	5	41.7	3	27.3	
Above normal (> 1.4)	6	50.0	7	63.6	[-30.2%; 27.3%]
Serum urea (mmol/L)					
Below normal (< 2.6)	0	0	0	0	
Normal range (2.6 – 7.0)	0	0	0	0	
Above normal (> 7.0)	12	100.0	11	100.0	[-25.9%; 24.3%]
Serum creatinine (umol/L)					
Below normal (< 64.0)	0	0	0	0	
Normal range (64.0 – 104.0)	0	0	0	0	
Above normal (> 104.0)	12	100.0	11	100.0	[-25.9%; 24.3%]

[#] Please note for the following variables, there was a response of 12 participants in the experimental group instead of 13 and 11 participants in the control group instead of 13, as one participant in each group did not come to the CAPD unit for biochemical measures (transport issues) and the one patient in the control group died before the intervention

[§] Please note for the following variable, there was a response of 8 participants in the control group instead of 11, as 3 blood results went missing (limited resources and limited time to repeat measurement)

The median changes in the biochemical measurement from baseline to post-intervention, were not significantly different between the two groups (Table 4.15), but there was a tendency for serum albumin to have decreased in the experimental group at the post-intervention assessment (95% CI for the median difference [-7.0; 0]).

Table 4.15: Comparison of the change in median biochemical measures within the two groups from baseline to post-intervention

Variable	Experimental Group (n=13)		Control Group (n=12)•		Experimental Group (n=12)#		Control Group (n=11)#		95% CI for the median difference
	Baseline				Post-intervention				
	Median	Minimum; maximum	Median	Minimum; maximum	Median	Minimum; maximum	Median	Minimum; maximum	
Serum albumin (g/L)	29.0	19.0; 39.0	29.0	15.0; 38.0	33.0†	21.0†; 37.0††	28.5†	8.0†; 37.0†	[-7.0; 0]
Serum sodium (mmol/L)	134.0	130.0; 139.0	135.0	132.0; 141.0	138.0	128.0; 142.0	139.0	134.0; 144.0	[-3.0; 4.0]
Serum potassium (mmol/L)	3.7	2.8; 5.2	4.1	2.5; 4.9	4.2	3.2; 4.9	4.2	2.9; 5.8	[-0.9; 0.7]
Serum phosphate (mmol/L)	1.4	0.7; 2.6	1.8	0.9; 2.4	1.5	0.5; 3.1	1.6	0.8; 2.7	[-0.5; 0.4]
Serum urea (mmol/L)	16.4	6.6; 33.7	20.3	13.2; 38.6	21.7	16.0; 37.3	21.3	8.6; 28.9	[-9.9; 3.0]
Serum creatinine (mmol/L)	890.0	316.0; 1422.0	760.0	400.0; 1745.0	863.0	447.0; 1414.0	1033.0	438.0; 1457.0	[-123.0; 316.0]

Please note for the following variables, there was a response of 12 participants in the experimental group instead of 13 and 11 participants in the control group instead of 13, as one participant in each group did not come to the CAPD unit for biochemical measures (transport issues) and the one patient in the control group died before the intervention

† Please note for the following variable, there was a response of 8 participants in the control group instead of 11, as 3 blood results went missing (limited resources and limited time to repeat measurement)

The changes in biochemical measures categorised according to recommendations, from baseline to post-intervention, were not statistically significant different between the two groups (Table 4.16).

Table 4.16: Comparison of the change in median biochemical categories between the two groups from baseline to post-intervention (NHLS, Frere Hospital)

Variable	Experimental group (n=13)		Control group (n=12)		Experimental group (n=12)[1]		Control group (n=11)[#]		95% CI for the percentage difference
	Baseline				Post-intervention				
Serum albumin (g/L)[§]									
Below normal (< 35.0)	12	92.3	11	91.7	9	75.0	7	87.5	[-35.4%; 24.3%]
Normal range (35.0 – 52.0)	1	7.7	1	8.3	3	25.0	1	12.5	
Above normal (> 52.0)	0	0	0	0	0	0	0	0	
Serum sodium (mmol/L)									
Below normal (< 135.0)	9	69.2	5	41.7	4	33.3	2	18.2	[-32.8%; 26.6%]
Normal range (135.0 – 147.0)	4	30.7	7	58.3	8	66.6	9	81.8	
Above normal (> 147.0)	0	0	0	0	0	0.0	0	0	
Serum potassium (mmol/L)									
Below normal (< 3.3)	3	23.1	1	8.3	2	16.7	2	18.2	[-32.8%; 26.6%]
Normal range (3.3 – 5.3)	10	76.9	11	91.7	10	83.3	8	72.7	
Above normal (> 5.3)	0	0	0	0	0	0	1	9.1	
Serum phosphate(mmol/L)									
Below normal (< 0.8)	2	15.4	0	0	1	8.3	1	9.1	
Normal range (0.8 – 1.4)	6	46.2	4	33.3	5	41.7	3	27.3	
Above normal (> 1.4)	5	38.5	8	66.7	6	50.0	7	63.6	[-36.5%; 28.2%]
Serum urea (mmol/L)									
Below normal (< 2.6)	0	0	0	0	0	0	0	0	
Normal range (2.6 – 7.0)	1	7.7	0	0	0	0	0	0	
Above normal (> 7.0)	12	92.3	12	100	12	100	11	100	[-27.8%; 24.3%]
Serum creatinine (mmol/L)									
Below normal (< 64.0)	0	0	0	0	0	0	0	0	
Normal range (64.0 – 104.0)	0	0	0	0	0	0	0	0	
Above normal (> 104.0)	13	100	12	100	12	100	11	100	[-27.8%; 24.3%]

[#] Please note for the following variables, there was a response of 12 participants in the experimental group instead of 13 and 11 participants in the control group instead of 13, as one participant in each group did not come to the CAPD unit for biochemical measures (transport issues) and the one patient in the control group died before the intervention

[§] Please note for the following variable, there was a response of 8 participants in the control group instead of 11, as 3 blood results went missing (limited resources and limited time to repeat measurement)

4.4.4 Efficiency of dialysis

Post-intervention the median weekly Kt/V and median creatinine clearance were recorded and the 95% CI for the median difference between the groups were calculated. The median weekly Kt/V was 1.6 in the experimental group (0.8 – 2.3) and 1.1 in the control group (0.8 – 1.9) and the median weekly creatinine was 40.2 in the experimental group (1.9 – 58.6) and 42.1 in the control group (1.6 – 49.5). No statistical significant difference was found in weekly Kt/V (95% CI for the median difference [-0.1; 0.8]) or weekly creatinine clearance (95% CI for the median difference [-10.4; 16.5]).

The adequacy of dialysis was interpreted as adequate or inadequate according to recommended standards for patients receiving CAPD (Table 4.17) (Moosa *et al.,* 2006). Only two participants (18.2%) in the experimental group received adequate dialysis in terms of the Kt/V formula. None of the participants in the study or control groups received adequate dialysis when based on the creatinine clearance.

Table 4.17: Difference in the adequacy of dialysis: post-intervention

Variable	Experimental group (n=11)[#]		Control group (n=9)[#]		95% CI for the percentage difference
	n	%	n	%	
Kt/V					
Inadequate dialysis (≤2.0)	9	81.8	9	100	[-47.7%; 14.5%]
Adequate dialysis (≥2.0)	2	18.2	0	0	
Creatinine clearance					
Inadequate dialysis (≤ 70)	11	100	9	100	[-25.9%; 29.9%]
Adequate dialysis (≥ 70)	0	0	0	0	

[#]Please note for the following variables, there was a response of 11 participants in the experimental group instead of 13 and 9 participants in the control group instead of 13, as these participants did not come to the CAPD unit for biochemical measures (transport issues) and the one participant from the control group died before the intervention

4.5 Summary

At baseline, the majority of the study population, consisting of 26 of the 28 patients receiving CAPD at Frere Hospital at the time of the trial were female; Black; unemployed or receiving a grant; and lived further than 50 km away from Frere Hospital, with two to three other people. Hypertension was the main cause, as well as the main comorbidity, of their renal failure, and most used ACE inhibitors, anti-anaemic drugs, calcium channel blockers, calcium carbonate (as antiacid), and folic acid supplements. Most had been receiving CAPD, as four exchanges per day, for five to eight months and had a HD line in place. None of the participants were underweight based on BMI, or wasted based on AMA (Table 4.1, 4.4 and 4.11); about a third was overweight/obese based on BMI. SGA nutrition assessment tool identifies less than 30% as mildly to moderately malnourished, while only one participant was severely malnourished. Serum albumin levels were below normal in more than 90% of participants and a third had edema of up to 2kg present. No participants had sodium or potassium levels above normal reference ranges for patients on RRT, while half had elevated serum phosphate levels. Serum urea level were more than double the upper limit of the normal range, and serum creatinine level was about eight times the upper limit of the normal range. Most participants had inadequate intakes of energy, protein, HBV protein, carbohydrate and fat. In this trial, supplementation with a protein powder, did not significantly impact on the nutritional status, assessed in terms of anthropometry, SGA nutrition assessment tool and biochemistry. Measurements at baseline, after one, two and three months, followed similar trends as that recorded post-intervention

4.6 Limitations and problems encountered during the trial

Unforeseen problems out of the researcher's control, which occurred during the trial included:

i. One participant from the control group died before the intervention started.
ii. The CRP was not determined in the trial due to limited funding at the hospital for this biochemical measurement.
iii. Some results for anthropometry, SGA nutrition assessment tool scores, biochemical measures and adequacy of dialysis were missing during the trial due to a number of factors. Ongoing transport strikes in the area of the trial prevented a few of the participants from coming to the hospital, and the researcher and the nurses were not able to go to the participant's houses due to the long distance and lack of resources to perform the tests away from the hospital. Insufficient time prevented the researcher from repeating the tests before the patients' next follow up at the hospital, as data was collected on monthly points.

iv. Some participants also forgot or were not physically able to come on their certain day and thus came one or two weeks before or after their planned date (which was spaced out evenly within the data collection period).

v. Dietary data measurements beyond month two was not collected due to time constraints, as the other data took longer than anticipated to collect.

vi. Serum cholesterol measurements beyond month two was not determined in the trial due to limited funding at the hospital to obtain this biochemical measurement on a monthly basis.

Chapter 5: Discussion

5.1 Introduction

This trial aimed to determine the effect of protein supplementation on the nutritional status of participants receiving CAPD during a randomised controlled clinical trial, conducted at Frere Hospital. The results are discussed in two sections. The first section profiles the socio-demographics, CAPD regime, medical history and nutritional status of the study population at baseline, and the second section interprets the changes that were observed in nutritional status over the intervention period.

5.2 Profile of the study population at baseline

The profile of the study population of patients receiving CAPD at Frere Hospital in the Buffalo City (BC) district of the EC, SA, is discussed regarding socio-demographic information, medical history, CAPD regime and nutritional status, based on anthropometry, SGA nutrition assessment tool, biochemical measures and dietary intake.

5.2.1 Socio-demographic profile

The median age of the study population of around forty years - 39.8 years in the experimental group (25 to 54 years old) and 37.2 years in the control group (24 to 51 years old). This agrees with the findings of other South African surveys in the patient population receiving CAPD (Isla *et al.,* 2014*;* Abdu *et al.,* 2011; Naicker, 2002). The young age of the study population, however, reflects the selection criteria for RRT in SA, as patients older than 60 years are not accepted onto the public sector chronic dialysis program , due to limited resources (Abdu *et al.,* 2011).

Although the literature reports that the incidence of ESRD is higher in males than females (Coresh *et al.,* 2007; Schrier, 2009), and other South African studies reported higher prevalence of male compared to female participants receiving CAPD (Isla *et al*., 2014; Abdu *et al.,* 2011; Naicker, 2002), most of the participants in this trial were female.The reason for the higher prevalence of female participants in this trial is not known.

Ethnicity is one of the four main risk factors which contribute to the progression of ESRD (Schrier, 2009). Two to three times higher risk for ESRD has been described in African American diabetic patients compared to white diabetic patients (Schrier, 2009). Most of the participants in the current trial were of black.

This may be related to the higher prevalence of hypertension, which is the leading cause of renal failure in patients, among black South Africans (Coresh *et al.,* 2007; Schrier, 2009) as discussed later. Other South African studies among the patient population receiving CAPD (Abdu *et al.,* 2011), report similar racial profiles; in a study on patients receiving CAPD in Gauteng, 86% of the participants were of black ethnicity (Abdu *et al.,* 2011).

Only a third of participants in both groups lived closer than 50 km from the dialysis clinic, while 15% in the experimental group and 25% in the control group lived more than 201 km away. This is similar to the results reported in a recent survey in Polokwane, Limpopo Province, SA. The main advantage of PD is that patients can perform CAPD at home, rather than having to go to dialysis units only situated in bigger centres, like patients receiving HD are required to do (Isla *et al*., 2014). This allows greater flexibility for daily activities and patients may even continue to work (Schrier, 2009).

Most patients relied on a grant as only source of income, and most participants were unemployed; which is similar to the employment rates for the CAPD population in the Limpopo Province, SA Isla *et al.* (2014). The EC ranked third in the country for unemployment rates according to the National Food Consumption Survey Fortification Base (Labadarios *et al.,* 2007), despite efforts to improve poverty rates by increasing the number of social grants to the poor. .

Although CAPD has many advantages over HD, including no need for vascular access, greater flexibility, and fewer cardiovascular complications (Moosa *et al*., 2006), the employment rate in this population receiving CAPD, was only about half that of the general population in the BC district (36.2%) (Stats SA, 2011). Similar statistics was seen in a Dutch population, where employment among participants receiving dialysis (35%) was also only about half of that in the general Dutch population (61%) (van Manen *et al.,* 2001). The latter study also further showed that the proportion of employed participants among the Dutch patients receiving CAPD, decreased from 48% to 40% over the duration of one year (van Manen *et al.,* 2001). Impaired physical and psychosocial functioning was observed as independent risk factors for this loss of employment (van Manen *et al.,* 2001). Van Manen *et al.* (2001) found that improvements in both physical and psychosocial functioning potentially prevent loss of employment in patients who were employed when they started dialysis. Griffin *et al.,* (n.d) found that, while participants receiving HD were more severely ill in terms of organ dysfunction and CRF complications, participants receiving CAPD appeared to show worse psychological adjustment.

Participants receiving HD were marginally less depressed, less anxious, and reported more positive moods, when compared to those receiving CAPD (Griffin *et al.,* n.d). One explanation suggested for this finding, is that patients receiving CAPD experience greater distress and isolation, due to lack of social support from other patients with CRF, and from health care professionals (Griffin *et al.,* n.d). Psychological stressors (such as lack of freedom, lack of control, and a feeling of loss) have been identified in a Swedish dialysis population (Lindqvist *et al.,* 2000). Renal supportive care is a dynamic, emerging concept aiming at meeting every day goals through the communication between the multi-disciplinary teams and patients with ESRD (Noble *et al.,* 2007). More research on the quality of life in patients with ESRD should be done in this population to further investigate the impact of treatment modality on social relationships and psychological adjustment, which also affect employment aspects (Griffin *et al.*, n.d).

5.2.2 Medical history

In the current study population, hypertension was the leading cause of ESRF and also the most prevalent co-morbidity as recorded from the participants' medical files.Most participants used medication to treat hypertension. The high prevalence of hypertention among the black participants in this study group, which included the entire population of CAPD patients at Frere Hospital, may be related to the high prevalence of hypertension that exist among the sub-Saharan African population (Arogundale & Barsoum, 2008).

According to participants' files, almost half of the participants suffered also from anemia, while a fifth had diabetes. Iron therapy medication to treat anemia was prescribed to most of the participants (65% of participants from both groups); regardless of whether anemia was recorded in the participants' file or not. Almost all of the diabetic participants were receiving medication to control diabetes (oral medication, and/or insulin). The majority (80%) of participants were using calcium carbonate supplements as a phosphate binder, and furosemide as a diuretic. Compliance to phosphate binders was not an objective of the trial, but the biochemistry results show poor control of phosphate levels and thus can be assumed that the compliance to the medication and low phosphate diet was poor or that the phosphate binders were ineffective. Compliance to furosemide was also not an objective of the trial, but the incidence of edema was present in many of the participants, proving that either the compliance to the diuretic was poor or that the diuretic was ineffective.

More than a half of the participants were using folic acid supplements. Folic acid therapy is believed to lower homocysteine levels in an effort to reduce cardiovascular disease in patients with ESRD, but the results have been inconclusive (Qin *et al.,* 2011). However, a meta-analysis performed by Qin *et al.,* (2011) showed that folic acid therapy can reduce cardiovascular risk in patients with ESRD by 15%.

5.2.3 CAPD regimen

Most participants in the current trialwere performing four daily exchanges; which is in line with the recommended guidelines (Schrier, 2009).

Compared to other SA studies, the median duration that the current study population had been receiving CAPD, namely five months (experimental group) to eight months (control group), was relatively short (Abdu *et al.,* 2011; Naiker, 2002). The causes may be multi-factorial and be related to the treatment modality or be system-related or patient-related (Chaudhary, 2011). It is, for example, important that both patient and the physician are educated on and comfortable with using the chosen modality, in order to successfully initiate and sustain CAPD (Chaudhary, 2011). Furthermore, one of the major causes for patients receiving CAPD, to switch to HD is peritonitis, which is most often experienced during the first 12 to 24 months of initiating CAPD (Chaudhary, 2011). The prevalence of peritonitis among patients receiving RRT at Frere Hospital, or among the current study population is not known.

Another factor which may cause patients receiving CAPD to switch to HD, is poor fluid and volume control. Careful management of volume status is required to sustain the patient receiving CAPD (Chaudhary, 2011). Excessive sodium and fluid intakes, inadequate dialysis prescription, catheter malfunction, and inadequate dietary guidelines are often causes of inadequate volume control (Chaudhary, 2011). As is discussed later, edema was present in a third of participants; while almost none of the participants were receiving adequate dialysis.

All patients need pre-dialysis counselling before CAPD or HD is initiated (Chaudhary, 2011). The pre-dialysis counselling helps patients choose, and encourage them to stay on a modality of RRT which is most suitable for them. The importance of counselling was illustrated in Hong Kong study where 50% of participants who were initially reluctant to start CAPD, agreed to this modality after pre-dialysis counselling were done (Lo *et al.,* 2001).

Similarly, close to half of participants in a United Kingdom study chose CAPD after proper counselling on both CAPD and HD was done (Little *et al.,* 2001). Psychological counselling and support can also prevent patients from switching unnecessarily between CAPD and HD (Chaudhary, 2011)..

Statistics at Frere Hospital from 2011 to 2012 indicate that approximately one patient receiving CAPD, has died every two months, which may also have contributed to the short median duration of CAPD among the study population. Low serum albumin levels are associated with high mortality rates (Fouque, 2007; Kopple, 1994). Almost the entire current study population had serum albumin levels below the normal reference ranges (35 g/L to 52 g/L), and more than 60% had serum albumin levels below 30g/L. In a recent retrospective study of patients receiving CAPD in the Polokwane between 2007 to 2012, serum albumin levels was also identified as a predictor of whether patients remained on CAPD or not (Isla *et al.,* 2014).

5.2.4 Nutritional status

Nutritional status has been highlighted as a very important issue in patients with ESRD during the past few years, as these patients are often malnourished (Mitch & Ikizler, 2010). The current approach of KDIGO in the assessment of a patient's nutritional status is a multi-dimensional approach (KDIGO, 2013). The anthropometry measurements, SGA nutrition assessment tool, biochemical measures and dietary intake are discussed.

5.2.4.1 Anthropometry measurements

i. Dry weight and BMI

Malnutrition and wasting is common among patients with CRF (Calvo *et al.,* 2002; KDOQI, 2000; Kooman *et el.,* 1992; Schreiber, 2001), and particularly significant in patients receiving CAPD (Abdu *et al.,* 2011; Burkart, 2002; Flanigan *et al.,* 1998; Naicker, 2003; Young *et al.*, 1991). It was therefore expected that the majority of the current study population would be undernourished. However, only one participant was underweight according to BMI (based on edema-free body weight). One third of participants in the trial were overweight and obese at baseline. In a Gauteng study, 60% of the participants were overweight and obese, but as BMI was not adjusted for edema, fluid status may have caused some overestimation (Abdu *et al.,* 2011). The median BMI in the current study population was however similar to that among participants receiving CAPD reported in a Durban study (Abdu *et al.,* 2011; Naiker, 2002).

A major disadvantage of using anthropometric measurements, such as the BMI, is the lack of standard reference values for an indigenous African population (Abdu *et al.,* 2011).

Analysis of worldwide trends in population BMI from 1980 to 2008 showed an increase of between 0.4-0.5 kg/m^2 per decade for males and females (Shisana *et al*, 2012) in the general population. The prevalence of overweight men and women in SA decreased to 44.6%, while the levels of obesity increased dramatically to 51.7% (Shisana *et al*, 2012). The high prevalence overweight and obesity among the participants receiving CAPD at Frere Hospital, may reflect the high prevalence of overweight and obesity in the surrounding population.

Another factor that may have also contributed to higher BMI in the current study population, was the relative short median duration on CAPD. Glucose which is absorbed from the peritoneal solutions contributes approximately 300-600kCal (1260-2520kJ) to daily energy intakes (Kopple & Mehrotra, 2003; Schrier, 2009). Therefore, it is common for patients to gain weight in the first 12 to 18 months after starting CAPD (Schrier, 2009).

ii. AMA

AMA is a value obtained from the combination of the MUAC and the TSF measurements. It is a good indication of lean body mass and thus of an individual's skeletal protein reserves (Hammond, 2008). More than half of the participants had a normal to above average AMA, which is similar to the findings of a study done in Gauteng where the majority (63%) of participants had an normal to above normal AMA (Abdu *et al.,* 2011). A third of the participants in each of the groups in this trial had AMA measurements that were below average, whereas only one participant in each group at month two had AMA indicative of wasting. A few participants presented with muscle wasting, despite normal BMI measurements. Factors contributing to wasting include decreased oral energy intake. Inadequate dietary intakes were observed in both groups and will be discussed later. Other factors contributing to wasting, which was not part of this trial's objectives, include anorexia (due to nausea, emesis, medication side effects, uremia); inflammation (due to co-morbidities and related to dialysis procedures); metabolic acidosis; endocrine disorders; and psychosocial factors (depression, low physical activity, loneliness and poverty) (KDOQI, 2006). Underdialysis also contributes to wasting and will be discussed in more detail later (KDIGO, 2013).

5.2.4.2 SGA nutrition assessment tool

The SGA nutrition assessment tool is a reliable predictor of cardiovascular risk in both male and female patients with CRF, although there are different opinions regarding the validity of the SGA nutrition assessment tool in populations receiving CAPD (KDOQI, 2000). According to the SGA nutrition assessment tool score, the majority of the participants in both groups were classified as well nourished. Less than one third of the participants in the experimental group and less than one sixth of the participants in the control group were classified as moderately malnourished. The findings of this trial were consistent with that of Young *et al*. (1991) who reported that based on the SGA nutrition assessment tool score, 32.6% of participants on CAPD, were mildly to moderately malnourished. A slightly higher percentage (44.9%) of Korean participants were reported to be mildly to moderately malnourished in a study by Chung *et al*. (1999).

Contrary to the current trial, other South African studies found higher prevalence of malnourishment based on the SGA nutrition assessment tool among patients on CAPD, tool. In Gauteng, Abdu *et al., (*2011) found that, according to the SGA nutrition assessment tool score, only 42% of participants were classified as well-nourished; despite 60% of participants having a BMI above the normal range; 50% of participants were moderately malnourished while 8% was severely malnourished, therefore noting a significant correlation between the SGA nutrition assessment tool score and anthropometric measurements (BMI and MUAC). Naicker (2002), using a different assessment tool, identified much higher prevalence of malnourishment (76.2%) their participants living in Durban. Similarly, a study among eighty one patients from India found that 50% of participants were moderately malnourished using the SGA nutrition assessment tool tool (Tapiawala *et al.,* 2006)

Only one participant in the current trial was classified as severely malnourished. This finding is similar to that of Young *et al*. (2001), who reported severe malnutrition among 8.0% of participants receiving CAPD from six dialysis centres in Europe and North America; and that of Chung *et al*. (1992) who reported severe malnoutrition in 2 % of Korean participants.

Some authors do not agree that SGA nutrition assessment tool is a sensitive or a reliable predictor of the degree of malnutrition (Mitch & Ikizler, 2010), and may differentiate malnourished patients from those with normal nutrition (Cooper *et al.,* 2002).

5.2.4.3 Biochemical measures

i. Serum albumin levels

A low serum albumin is considered the strongest predictor of mortality in patients with CRF (Beddhu *et al*., 2002; Lacson *et al.,* 2009), even compared to other risk factors associated with a higher mortality, such as hypertension, hypercholesterolemia, diabetes mellitus and obesity (Beddhu *et al*., 2002; Lacson *et al.,* 2009). The disadvantage of using serum albumin, is that, as a negative acute phase reactant, levels are also decreased in response to inflammation and metabolic stress (Kalantar-Zadeh *et al*., 2011). CRP, another acute phase protein, may be used as a marker of infectious diseases, inflammatory disorders, malignancy, and tissue trauma (Litchford, 2006), but was not obtained in this trial due to lack of resources in the hospital.

More than ninety percent of participants in this trial had decreased serum albumin levels, and this is a much higher prevalence than that reported in other South African studies on the CAPD population. Abdu *et al.,* (2011) found that only 25% of a study population in Johannesburg, and Naicker (2002) that only 14% of a study population in Durban, had decreased serum albumin. Abdu *et al.,* (2011) found no correlation between the serum albumin level and SGA nutrition assessment tool score.

Serum albumin is also affected by hydration status. As a third of participants had edema present at the baseline assessment (to maximum of 2.5kg; despite more than 80% receiving diuretics), dilution of serum albumin may have confounded the albumin levels in this trial. Further reasons for the high prevalence of hypoalbuminea also needs to be explored in future studies, in which CRP should also be measured to assist in the interpretation.

ii. Serum sodium and potassium levels

Less than three quarters of the participants in the experimental group, and less than half of the participants in the control group, had below normal serum sodium levels. Water overload or overhydration in patients with CRF, results in hyponatremia (Arroyo, 2008). About a third of the participants had edema present or were overhydrated at the baseline assessment and may have contributed to below normal serum sodium levels.

iii. Serum phosphate levels

Inadequate dialysis may also have contributed to the fact that serum phosphate levels were elevated in 50% of the overall study population.

Most participants were using calcium carbonate antiacids as phosphate binders. Compliance to phosphate binders was not an objective of the trial, but the biochemistry results show poor control of phosphate levels and thus can be assumed that the compliance to the medication and low phosphate diet was poor or that the phosphate binders were ineffective.

Sixty percent of ingested phosphorus is absorbed from the gut, and is further increased with simultaneous intake of active vitamin D (Argarwal, 2009). One gram of protein contains on average 12 – 16 mg of phosphorous, and patients receiving dialysis need to eat a minimum of 1.2 g/kg/day protein, in which a minimum of 800 – 1000 mg of phosphorous will be ingested and therefore it is not possible to control hyperphosphatemia with diet alone (Argarwal, 2009). The availability of different phosphate binders differs locally and internationally, such as aluminium hydroxide, calcium citrate, magnesium carbonate, calcium carbonate, calcium acetate, lanthanum carbonate, Sevelamer-HCl and Sevelamer carbonate (KDIGO, 2013).

Serum phosphate above the recommended range is associated with mortality and experimental data suggests it is directly related to bone disease, vascular calcification and cardiovascular disease (KDIGO, 2013). There is insufficient evidence that any specific phosphate binder significantly impacts on patient-level outcomes (KDIGO, 2013). A Cochrane meta-analysis of 60 RCTs or quasi-RTCs (with a total of 7631 participants) assessed the effects of different phosphate binders and concluded all the available phosphate binders reduce serum phosphate in comparison to the placebo (Navaneethan *et al*., 2011). This Cochrane review shows that no data, to date, supports the superiority of novel non-calcium binding agents for patient-level outcomes, such as all-cause mortality and cardiovascular end points in patients with CKD (Navaneethan *et al*., 2011).

iv. Serum urea and creatinine levels

The serum concentrations of the waste products, urea and particularly creatinine, were increased above normal reference ranges in almost all of the participants. The median serum urea level of the experimental group was twice, and that of the control group, three times the upper limit of the normal range. The mean serum creatinine level was about eight times the upper limit of the normal range in both groups. This may be related to the fact that, as discussed later, only one of the participants in the entire study population were being adequately dialysed.

v. Serum cholesterol levels

A relationship between low serum cholesterol and increased mortality has been showed as an independent predictor of mortality in patients receiving HD, but has not been observed in patients receiving CAPD (Avram *et al.,* 1995; De Lima *et al.*, 1995; Goldwasser *et al.*, 1993). In the current trial, serum cholesterol was elevated above normal in all of the participants in the experimental group and in a third of the participants of the control group. Patients with ESRD (and a GFR of less than 15ml/min/1.73m^2) are at the highest risk of a CVD event and these events occur at a younger age, suggesting that CRF promotes CVD at an accelerated rate (KDIGO, 2013). Albuminuria is associated with duration and severity of hypertension; an adverse lipid profile with higher levels of total cholesterol (as seen in this trial), triglycerides, and lipoprotein (a) (KDIGO, 2013). Weight loss in obese patients with CRF can reduce the decline in GFR, proteinuria and blood pressure (KDIGO, 2013). Obesity enhances the risk for glomerular hyperfilteration and hyperperfusion, and elevated albumin excretion is often seen in obese non-diabetic patients (Ide & Akani, 2011). KDIGO (2013) also recommends patients with CKD receive expert dietary advice and information in context of an educational program, tailored according to the severity of CKD and the need to change salt, phosphate, potassium and protein intake where indicated.

The Study of Heart and Renal Protection (SHARP), which is the largest RCT in patients with CRF to date, demonstrated that a lipid-lowering strategy including fixed dose Simvustatin and Ezetimibe resulted in a 17% reduction in atherosclerotic events compared to the placebo (Baigent *et al.,* 2011). Less than one third of the participants in the experimental group, and less than one sixth of the participants in the control group, were receiving cholesterol and triglyceride modifiers (Simvustatin) as documented in the participants' file. Although many guidelines acknowledge that CRF is associated with an increase in CVD risk, assessing for CVD risk is still not included in many assessment tools, due to lack of available ethnicity and regional specific tools (KDIGO, 2013). The under prescription/underutilisation of cholesterol lowering drugs could have been highlighted in this population group, had there been a specific assessment tool for CVD risk.

5.2.4.4 Dietary intake

i. Energy intake

Adequate energy intake for patients receiving CAPD is defined as 30 to 35 kCal/kg (KDOQI, 2006). More than two thirds of participants in both groups had inadequate energy intakes of less than 30 kCal/kg. Inadequate intakes of all the macronutrients were also reported as discussed below.

This was surprising in light of the fact that the majority of participants had normal/above normal BMI and normal AMA measurements. Abdu *et al*., (2011) found that among a study population receiving CAPD in Johannesburg, SA, 49% had inadequate energy intakes. Dietary intake may have been underreported, despite the use of the MRC Food Flash Cards and Food Photo Manual to increase the reliability of the reporting process (Steyn & Senekal, 2005).It is a well-acknowledged fact that in the 24-hour recall participants with lower observed intakes tend to over-report and those with higher observed intakes tend to under-report their past dietary intakes (Ferguson *et el*., 1995; Gewa, Murphy & Neumann, 2009).

Dietary behaviour and eating patterns are also influenced by nutritional knowledge and beliefs (Ma *et al.,* 2003). Surveys have found that the general South African population lack adequate health and nutrition knowledge, despite an improved level of education in the past few years (Kruger *et al.,* 2002; Mchiza, 2008, Shisana *et al.*, 2013; Steyn *et al.,* 2000). Non-adherence to dietary prescriptions is a common problem in patients with CRF and is associated to serious complications, such as calcifications (phosphate and phosphate binder non-adherence); cardiac arrhythmia (potassium non-adherence); fluid overload and heart failure (fluid and sodium non-adherence); and PEW (Herselman, 2008). The prevalence of non-adherence in patients receiving dialysis is reported as between 30-74% for fluid restrictions, 2-39% for potassium restrictions, and 9-57% for phosphorous restrictions (Denhaerynck *et al.,* 2007). Recording dietary behaviours was not an objective of this trial, but further research is needed to improve researchers understanding of the factors that predict adherence to dietary prescriptions and may improve the quality of life and survival of patients with CRF in a South African setting (Herselman, 2008).

ii. Protein intakes

Although the median intake of protein was sufficient, with the experimental group consuming 1.0 g/kg (excluding the protein powder supplementation of 0.65g/kg) and that of the control group consuming 1.2 g/kg, more than half of the study population had inadequate protein intakes. The intake of HBV protein was below the recommended 50% of total protein intake, in about two thirds of the study population (KDOQI, 2006). This constitutes a lower intake of protein than reported for a study population receiving CAPD in the Johannesburg study (Abdu *et al.*, 2011). In the latter study, participants also consumed a higher percentage (60%) of HBV protein, which is in line with the KDOQI recommendations (Abdu *et al.,* 2011).

HBV protein includes red meat, fish, chicken and eggs, which are usually more expensive than plant-based alternatives, which in turn do not contain the full spectrum of essential amino acids and therefore are not generally sources of HBV protein (KDOQI, 2006).

According to SANHANES-1 (Shisana *et al.,* 2013), in 2012, overall 54% of households in SA were food insecure; 28% were at risk for hunger and 26% experienced hunger The EC province has the highest prevalence of food insecurity and hunger in SA (Shisana *et al.,* 2013). The current study population, being largely unemployed and reliant on grants, seem to have little money available for food, particularly for the more expensive sources of HBV.

iii. **Carbohydrate intake**

In about half of the study population, carbohydrates failed to make up at least 50% of total energy. The median intake of carbohydrates through food alone for the experimental group was lower than that of the control group. Adequate carbohydrate intake for patients receiving CAPD, is defined as 50 – 60% of TE (KDOQI, 2006). Steyn & Nel (2006) found that women living in rural areas in SA, had a significantly higher mean carbohydrate intake compared to those living in urban areas, therefore the carbohydrate intake in the current trial, where most of the participants were living in the rural EC, may have been expected to be higher than what was recorded. There may have been underreporting, as discussed. Peritoneal solutions used by this study population contain glucose, which is absorbed through the peritoneal membrane, and contributed to the total carbohydrate intake (Schrier, 2009). This may have compensated for some of the apparent deficit in dietary carbohydrate intake. The reported intake of dietary carbohydrates is also actually slightly higher in the experimental group than reported as the *Protifar* powder also contains some carbohydrates, typically 1.2 grams carbohydrate per 100g powder- therefore this additional carbohydrate intake from the supplement varied according to the participant's weight from baseline (supplemented at 0.65g/kg protein powder).

iv. Fat intake

In more than half of the study population fat intakes failed to make up at least 25% of TE, adequate fat intake is defined as 25 – 35% of TE (KDOQI, 2006). Steyn & Nel (2006) found that urban women had a statistical significant higher dietary fat intake of 29.1% of TE, compared to that of rural women at 15.6% of TE. The SANHANES-1 (2012) report indicated that the mean dietary fat intake was the lowest in the EC province; the inadequate fat intake of the study population therefore, may reflect the low dietary intake recorded in the EC region by recent literature (Shisana *et al.,* 2013).

The reported intake of dietary fat is also actually slightly higher in the experimental group than reported as the *Protifar* powder also contains some fat, typically 1.6 grams carbohydrate per 100g powder- therefore this additional fat intake from the supplement varied according to the participant's weight from baseline (supplemented at 0.65g/kg protein powder).

5.2.5 Summary of baseline findings

Participants were mainly relatively young, black African women, who relied on grants as their main source of income. According to the participant files, hypertension was the leading co-morbidity, which is consistent with literature on patients with CRF. In contrast to other SA studies, the duration that the participants had been receiving CAPD was relatively short. Unlike international studies, but similar to other South African studies, BMI and AMA measurements in the higher than normal ranges were reported in both groups. According to the SGA nutrition assessment tool scoring system, the majority of participants were classified as less malnourished than those in other studies done in SA. Despite these findings suggesting better nutritional status among these participants than what is generally reported for patients receiving CAPD in international studies, serum albumin levels were generally low. Energy and macronutrient intakes were mostly inadequate compared to the KDOQI (2006) recommendations. Almost the entire study population had decreased albumin levels and elevated levels of waste products and phosphate, which increases the risk of mortality and osteodystrophy in this population.

5.3 Effect of the protein supplementation on nutritional status

At baseline, no statistically significant differences were recorded between the experimental group and the control group in the medians for data regarding socio-demographics, medical histories, mediation use, CAPD regime or nutritional status based on anthropometry, SGA nutrition assessment tool, biochemistry or dietary intakes. Subsequently the experimental group was supplemented with protein powder, while the control group received the standard care, which was not a placebo powder. No placebo powder was given to the control group, as the investigators wanted to see the direct effect of the protein powder, which is a limitation of the study. Both groups were followed up and nutritional status was recorded at the end of month one, two and three and at the end of the trial. At each point of data collection, and at the end of the trial, the medians for data regarding anthropometry, SGA nutrition assessment tool, and biochemistry were recorded and compared between the two groups. At the end of the trial the median change in these parameters from baseline was compared between the two groups to access the success of the trial.

5.3.1 Anthropometry measurements

5.3.1.1 Dry weight and BMI

0ver the course of the trial, the median edema-free body weight of both the experimental group and the control group increased slightly. At the end of the trial, the median dry weight of the experimental group (69.4 kg) was 4.2 kg higher than at baseline, and that of the control group (67.9 kg) was 3.8 kg higher than at baseline. The median change in dry weight from baseline was however, not statistically significant between the groups.

As BMI is weight/height^2, very little change occurred in the median BMI during the trial At the end of the trial, the median BMI of the experimental group (25.1 kg/m^2) was 0.6 kg/m^2 higher than at baseline, and that of the control group (24.3 kg/m^2) was 1.3 kg/m^2 higher than at baseline. The median change in dry weight from baseline was however, not statistically significant between the groups.

5.3.1.2 AMA

Similarly the median AMA increased slightly in the experimental group over the trial period, while in the control group there wasa small decline in AMA At the end of the trial, the median AMA of the experimental group (53.3 cm^2) was 7.8 cm^2 higher than at baseline, and that of the control group (45.5 cm^2) was 5.2 cm^2 lower than at baseline. The median change in AMA from baseline was however, not statistically significant between the groups.

Although not statistically significant, the supplementation with protein powder may have had a clinical benefit in improving the anthropometric measurements.

5.3.2 SGA nutrition assessment tool

The same trend was also noted in the classification based on SGA nutrition assessment tool scoring. Although the majority of the participants in both the experimental group and the control group were classified as well-nourished at baseline, at the end of the trial the median percentage of participants that were classified as well-nourished, was 30.8% higher in the experimental group, and 4.6% lower in the control group. The median change in SGA nutrition assessment tool classification from baseline was not statistically significant between the groups, although the experimental group may have had a clinical benefit from the supplementation.

5.3.3 Biochemical measures

5.3.3.1 Serum albumin levels

During the trial the median serum albumin showed a small increasing trend in the experimental group and small decreasing trend in the control group. At the end of the trial, the median serum albumin levels of the experimental group (33 g/L) was 2g/L higher than at baseline, and that of the control group (28.5 g/L) was 0.5 g/L lower than at baseline. The median change in serum albumin levels from baseline was however, not statistically significant between the groups.

The disadvantage of using serum albumin is that it is a negative acute phase reactant that decreases in response to infectious diseases, inflammatory disorders, malignancy, and tissue trauma (Kalantar-Zadeh *et al*., 2011). Serum levels of CRP, which is a positive acute phase protein which increases under similar circumstances (Litchford, 2006), and which can therefore be used as an easily obtained marker, was unfortunately not available in this trial, due to lack of resources in the hospital.

Serum albumin is also affected by hydration status as discussed for the baseline findings. From baseline and throughout the trial, edema was present in between 8% and 46% of participants in the experimental group and in between 33% and 50% of the control group. The prevalence of edema were not significantly different between the groups, except at the end of month three when significantly more participants in the control group presented with edema than in the experimental group. The variation in edema prevalence in the study population may therefore have confounded the serum levels of albumin, as well as that of the other biochemical variables included in the trial. The current study population was however too small to investigate any associations between the prevalence of edema and these biochemical measures. Although not statistically significant, the supplementation with protein powder may have had a clinical benefit in improving the serum albumin levels. If the trial was longer, the study group was larger, or the protein supplement dosage was higher, a more significant change in serum albumin levels may have been observed.

In spite of the trends, the median serum albumin remained well below normal reference ranges in both the experimental and control groups during the course of the trial. Low serum albumin is the strongest measure of mortality in patients with CRF (Lacson *et al.,* 2009), even when comparing it to other risk factors associated with a higher mortality, such as hypertension, hypercholesterolemia, diabetes mellitus and obesity (Lacson *et al.,* 2009).

Studies have found that a change in serum albumin of a mere 1g/L over a time span of a few months, is associated with an increase or decrease in survival rate (Kalantar-Zadeh *et al*., 2004).Possible explanations were not clear from this trial and needs to be explored in future. Future trials should also assess CRP values and find ways to correct the serum biochemistry for edema.

5.3.3.2 Serum sodium and potassium levels

Serum sodium and potassium levels remained well controlled throughout the trial, despite inadequate dialysis in almost the entire study population. From baseline, throughout the course of the trial, the median serum sodium levels of the experimental group remained at the lower limit of the normal reference range for patients with CRF and then slightly increased at the end of the trail. The median change in serum sodium levels from baseline was not statistically significant between the groups. Serum potassium levels in the experimental and control groups increased slightly at the end of the trial. As discussed above, edema may have influenced the lower serum sodium and potassium levels in some participants.

5.3.3.3 Serum phosphate levels

Throughout the trial the median serum phosphate levels remained at the upper limit and above, of the normal reference range in both the experimental and the control groups. In the control group the percentage of the participants with median serum phosphate levels above normal, was found in around two thirds of the group throughout the trial. The median change in serum phosphate levels from baseline, and the median change in the percentage of participants with elevated phosphate levels, was not statistically significant between the groups. Therefore, it can be concluded that the protein powder supplement did not significantly contribute to elevated serum phosphate levels in the experimental group. As discussed at baseline the elevated serum phosphate levels in the entire study population throughout the trail, may be related to non-compliance to the phosphate binders, as well as the fact that almost no one of the study population was being adequately dialysed. Dietary intakes of protein and phosphate rich foods are also variables that influence serum phosphate levels. However as the dietary data indicates at baseline, and after one and two months, median protein intakes in both groups were within the recommendations for patients receiving CAPD, and even lower. No analysis was performed with regard to how well the study group were adhering to phosphate-restricting dietary guidelines.

Most participants were using calcium carbonate antiacids as phosphate binders. Compliance to phosphate binders was not an objective of the trial, but the biochemistry results show poor control of phosphate levels and thus can be assumed that the compliance to the medication and low phosphate diet was poor or that the phosphate binders were ineffective. Serum phosphate above the recommended range is associated with mortality and experimental data suggests it is directly related to bone disease, vascular calcification and cardiovascular disease (KDIGO, 2013).

5.3.3.4 Serum urea and creatinine levels

The median serum concentrations of the waste products, urea and creatinine, were increased and above the normal reference ranges in all of the participants, from baseline to the end of the trail. The median serum urea level of the experimental and control groups both remained at around three times the upper limit of the normal reference range throughout the trial. The median serum creatinine level remained at about eight times the upper limit of the normal range in the experimental group, and at ten times the upper limit of the normal range in the control group, throughout the trial.

Dietary intakes of protein rich foods may also influence serum creatinine and urea levels. However, as as discussed above, median protein intakes in this study population were within the recommendations for patients receiving CAPD in both groups. Dietary intake was not recorded at the end of the trail and in-depth dietary analysis did not form part of the objectives of this trial.

5.3.3.5 Serum cholesterol levels

At baseline the median serum cholesterol levels were elevated well above the normal reference range in the experimental group at the end of one month the median had decreased to within the reference ranges and then further declined to the end of the second month. At baseline the median serum cholesterol levels of the control group were high, after which it decreased towards the end of the first month, and increased again during the second month. The serum cholesterol measurements beyond month two was not determined in the trial due to limited funding at the hospital to obtain this biochemical measurement on a monthly basis. The reason for the normalisation of these serum cholesterol levels in the experimental group within one month of starting the protein powder supplementation, is not known. The half-life of cholesterol in the brain is between six months and 5 years, while the half-life of plasma or serum cholesterol is only a few days (Orth & Bellosta, 2012).

5.3.4 Dietary intakes from baseline to the end of the second months

Dietary data was only documented until the end of the second month due to logistical difficulties as explained before.

5.3.4.1 Energy intake

While there was no statistical significant differences between the two groups regarding energy and macronutrient intakes at baseline and after the first month, at the end of the second month energy intakes and fat intakes were significantly higher in the control than in the experimental group. Although underreporting as discussed before may have occurred, protein powder supplements have also been reported to cause adverse gastrointestinal effects, which may have caused participants in the experimental group to cut back on food (Jeloka *et al.,* 2013). Jeloka *et al.* (2013) supplemented patients receiving CAPD or HD, with whey and egg albumin protein supplements, but found that many of the participants did not tolerate the supplements due to bloating, nausea, vomiting and anorexia. Bammens *et al.* (2004) has shown that protein digestion and absorption is impaired in the small intestine of patients with ESRD, as well as in patients receiving CAPD or HD.
Jeloka *et al.* (2013), suggests that poor protein digestion and absorption, together with gastric acid suppressing drugs, and the protein load contributed by extra protein supplements, may cause fermentation of undigested proteins. This may result in the formation of toxic metabolites, which cause adverse effects. In the current trial, though compliance remained good (> 80%), some participants did report that they did not tolerate the protein powder well. The supplement may also have has suppressed apetite.

Similar to baseline, more than two thirds of participants in both groups had inadequate energy intakes of less than 30 kCal/kg throughout the trial, up to the last measurement taken after the second month. The median energy intakes were higher in the control group compared to the experimental group over the intervention period; and the energy intake decreased from baseline in the experimental groupand increased in the control group. This may possibly support the theory that the experimental group may have cut back on their food intake.

5.3.4.2 Protein intakes

No statistical significant difference was reported between the two groups for median dietary protein intake at any point of data collection. Similar to baseline median protein intakes for both the experimental and the control groups remained below the recommended 1.2 g/kg at months one and two in the majoririty of the particicpants.

More than three quarters of the participants in the experimental group and all of the participants in the control group had inadequate protein intakes of less than at month one of the intervention. \ More than three quarters of the participants in the experimental group and just less than three quarters of the participants in the control group had inadequate protein intakes of less than 1.2g/kg at month one of the intervention.

Similar to baseline, the intake of high biological value protein, expressed as less than 50% of protein intake (KDOQI, 2006), also remained below recommendations in most of the participants in both groups. The mean protein intake decreased in both groups over the intervention period. This trial was not blinded, therefore participants in the experimental group knew that they were receiving a protein powder supplement.

Most of the participants were unemployed or relied on a grant as a source of income, and they have little money available for expensive protein food. It is possible that they may have cut back on protein rich foods, which are generally the more expensive options.

5.3.4.3 Carbohydrate intake

The carbohydrate intakes improved from in the first and second months of the intervention and at these time points the minority of the participants in both groups had inadequate carbohydrate intakes of less than 50% of TE. These results are similar to that reported by Steyn & Nel (2006), who found that women living in rural areas in SA had significantly higher mean carbohydrate intake compared to those living in urban areas.

5.3.4.4 Fat intake

Most of the participants in both groups had inadequate fat intakes of less than 25 % of total energy (KDOQI, 2006). The median fat intakes increased from the first to the second month of the intervention, where the experimental and control group's median fat intake increased The median fat intake in month two was statistically different beteen the two groups. The worst compliance to dietary supplements was seen in the second month of the intervention; and it is therefore unlikely that this influenced the statistical significant difference between groups when comparing energy and fat intakes.

Another possible reason for the statistical significant difference between the two groups for dietary energy and fat intakes at month two of the intervention, is that the participants in the experimental group may have used the protein powder supplements to replace their usual food intake. Wilson *et al.* (2006) found that an inverse relationship existed between nutritional status and food insecurity of patients receiving HD at clinics in Louisiana, United States of America. Patients were examined for nutritional status by SGA nutrition assessment tool score and for food insecurity with the US Department of Agriculture Household Food Security Survey Module (Wilson *et al.,* 2006). Race significantly predicted food insecurity (β = 0.248; P = .019), with black patients being more food insecure than white patients. Furthermore, a significant positive relationship was found between the level of education and the SGA nutrition assessment tool scores (β = 0.222; P = .037) (Wilson *et al.,* 2006). Wilson *et al.* (2006) found that their patients were more food insecure (16%) than the national average of 11.7%. Similarly, most of the participants in this trial were of black ethnicity. Wilson *et al.* (2006) therefore suggest that food security needs to be added to the nutritional assessment of patients receiving dialysis.

As previously discussed in the socioeconomic profile of the participants, most of the participants in both groups relied on a grant as a source of income. Food insecurity may have played a major role in this trial, particularly in the experimental group, who may have replaced their dietary intake with the protein powder supplements. This may explain the fact that experimental group's energy and macronutrient intakes decreased during the intervention period.

5.3.5 Record of protein supplementation

Patients undergoing maintenance dialysis who are unable to meet their protein and energy requirements with food intake for an extended period of time, should receive nutritional support (KDOQI, 2006). If all the patient's complications with dialysis have been resolved, and there is still no increase in the patient's appetite and food intake, nutritional supplementation may be necessary (Bossola *et al.*, 2005; Kantar-Zadeh *et al.,* 2011; Kopple, 1994).

The compliance to protein powder was generally good in the experimental group. The best compliance was in the last month (90.5%), while the worst compliance was in the second month (82.4%) of the intervention. Many studies, however, indicate that the patients receiving CAPD are either noncompliant or intolerant to dietary supplements (Aguirre-Galindo *et al*., 2003; Eustace *et al*., 2000; Heaf *et al.* 1999; Kalantar-Zadeh *et al*., 2011; Shimomura, Tahara & Azekura, 1993; Teixidó-Planas *et al*, 2005).

Better tolerance and assumed adherence to these supplements have been reported with egg-albumin based supplements or calcium caseinate supplements, compared to standard oral supplements (González-Espinoza *et al*., 2005; Teixidó-Planas *et al*, 2005; Aguirre *et al.,* 2003; Heaf *et al.,* 1999). Protein supplements can also make patients feel unwell due to adverse effects of protein powder on the gastrointestinal systems. This may also cause them to cut back on certain foods (Jeloka *et al.,* 2013). Jeloka *et al.* (2013) supplemented patients receiving CAPD and HD with whey and egg albumin protein supplements, but found that many of their patients did not tolerate the supplements due to bloating, nausea, vomiting and anorexia. Reasons for missing the protein powder supplements in this trial were not very specific and participants gave general reasons, such as only being able to tolerate half the protein supplements, instead of more specific reasons found by Jeloka *et al.*

Bammens *et al.* (2004) has shown that protein digestion and absorption is impaired in the small intestine of patients with ESRD and in patients receiving both CAPD and HD. According to Jeloka *et al.* (2013), it is likely that poor protein digestion and absorption, together with gastric acid suppressive drugs and protein load due to extra protein supplements may lead to an increase in fermentation of undigested proteins which results in toxic metabolites and may be the actual pathogenesis of adverse effects when supplementing patients receiving CAPD and HD with protein supplements. This theory may explain why certain patients in this trial were intolerant to the protein powder supplements.

Reasons for non compliance to the protein supplements in this trial was very generalised, and included that the participant: “was only able to tolerate half a bag of protein powder given”; “was sick or felt physically too cold to ingest the protein powder”; “generally forgot to include the protein powder into his/her meal plan”; “was out of town or in hospital”; or “was fluid overloaded”. These reasons should be addressed when planning future studies in SA, as many stem form apparent misconceptions that participants regarding supplementation and the effect on their overall nutritional status.

5.3.6 Efficiency of dialysis

Only two participants in the experimental group and none in the control group received adequate dialysis in terms of the Kt/V formula, while none in either of the groups received adequate dialysis in terms of creatinine clearance. The adequacy of dialysis was not significantly different between the two groups.

These results are similar to that of a study in Gauteng, where only 19.2% of participants were receiving adequate dialysis (defined as a Kt/V more than 2.0) and 62.8% received adequate dialysis (defined as a Kt/v more than 1.7) (Abdu *et al.,* 2011). Peritoneal transport status is one of the main determinants of dialysis adequacy and dialysis-related complications in patients with ESRD receiving CAPD (Sezer *et al.,* 2005), while under-dialysis also contributes to wasting.

5.3.7 Summary of the effect of the trial

The mean BMI and AMA increased slightly in the experimental group from the baseline assessment; and decreased slightly in the control group, although this was not statistically significant. The control group had a tendency to lose weight and lower percentiles for AMA than the experimental group. The effect of protein powder supplementation therefore showed a clinical benefit of weight gain and an improvement and higher AMA in the experimental group. The majority of participants were well nourished according to the SGA nutrition assessment tool scoring system, which was different to other studies done in SA. The experimental group achieved better SGA nutrition assessment tool scores than the control group when comparing results from baseline to post-intervention, although this was not statistically significant; and therefore benefited from the protein powder supplementation. No difference was reported between the groups for biochemical parameters, though there is a tendency for the experimental group (who received the protein supplementation) to obtain higher serum albumin than the control group. While serum sodium and potassium levels seemed to be well controlled with values ranging between low to normal in both groups, serum phosphate levels were elevated in half of the experimental group and two thirds of the control group; which could be due to a higher phosphate intake (meat and protein powder supplementation) or non-compliance to phosphate binder medication. Most of the participants in both groups had inadequate dialysis when comparing the Kt/V and creatinine clearance with recommended ranges; which was similar to another study in SA (Abdu *et al.,* 2011; KDIGO, 2013).

5.5 Limitations of the trial

The limitations of the trial will be discussed from the baseline assessment, intervention period and post-intervention.

This sample of participants represented the patients receiving CAPD of Frere Hospital only, which included East London and surrounding areas. Not all patients receiving CAPD in the EC region were used due to logistical and time constraints.

A small sample size of the population could have affected the results as there were only 13 participants in each group; however the whole population of patients receiving CAPD at Frere Hospital was used. These low numbers reflects the low number of patients with CRF in SA on RRT that receive CAPD (Abu-Aisha & Elamin, 2009). The percentage of patients receiving CAPD (47%) at Frere Hospital compared to patients receiving HD, is higher than the national average of 32% (Abu-Aisha & Elamin, 2009).

Thus the small sample size of the group represents almost half of the patients with CRF that were receiving RRT at Frere Hospital at the time of the trial. Other clinical trials in the population receiving CAPD tend to also have small sample sizes (Abdu *et al.,* 2011).

The mean duration of participants receiving CAPD was relatively short. Due to the short mean duration of participants receiving CAPD, more research on the quality of life in patients with ESRD should be done to further investigate the impact of treatment modality on social relationships and psychological adjustment, which has an effect on employment aspects, as well as unnecessarily changing modalities from CAPD to HD (Griffin *et al.,* n.d). The working situation and facilities available for participants who had part time or full time employment was not obtained as it was not an objective of the trial; but could have provided insight into the work place and whether there is a room to do the exchange, as well as sufficient storage space; which is a big barrier for these participants being employed.

Another factor which can shorten the duration of CAPD (and switching to HD) is poor fluid and volume control. The edema present in the participants during the trial was recorded throughout the trial and showed numerous participants with edema. Most of the participants in both groups were also receiving inadequate dialysis, and thus could also impact the higher prevalence of edema. The rate of peritonitis in these participants was not recorded as it was not an objective in the trial, but which may have had an effect on the short mean duration of participants receiving CAPD. One of the major causes for a patient receiving CAPD to switch to HD is peritonitis, which is especially seen in the first 12 – 24 months of initiating CAPD (Chaudhary, 2011).

BMI is not specific to the ESRD population and thus the BMI is compared to the standard values for a general population according to KDIGO (2013); there is a need for more specific BMI reference ranges for patients with ESRD.

It would be interesting to repeat this study in the same sample of participants as weight gain is experienced 12-18 months after CAPD has started due to the absorption of glucose through the peritoneal membrane on a daily basis and the mean duration of CAPD in this trial was relatively short (Schrier, 2009).

Low serum albumin levels are associated with high mortality rates (Fouque, 2007; Kopple, 1994). More than 60% of this study population had a serum albumin of less than 30g/L. Statistics at Frere Hospital over the previous year (2011-2012) indicate that approximately one patient receiving CAPD has died every two months. Serum albumin levels will decrease in a response to inflammation, as it is a negative acute phase reactant such as the CRP measurement; and this measurement was not obtained in this trial due to lack of resources in the hospital (Kalantar-Zadeh *et al*., 2011). The researcher could not control the number of participants lost in the trial due to CAPD being stopped (death or medical practitioner's decision to stop CAPD). One participant in the control group died before the intervention trial started; one participant in the experimental group changed from CAPD to HD during the intervention, and one participant in the control group had transport issues during transport strikes in the EC region over December 2012, preventing him from coming to the CAPD dialysis unit. Both these participants were thus excluded from the final follow-up assessment.

A statistical significant difference was noted between the two groups during month two for serum potassium, where the serum potassium was significantly higher in the control than in the experimental group. The reason for this difference could be due to a higher dietary potassium intake, but this was not an objective of the trial. The dietary intake parameters measured did not include electrolyte intakes, but rather focused on energy, protein, carbohydrate and fat intake. Serum phosphate levels were elevated in half of the experimental group and two thirds of the control group at post-intervention; which could be due to a higher phosphate intake (meat and/or protein powder supplementation) or non compliance to phosphate binder medication.This trial should have also included and analyzed the dietary potassium, phosphate and sodium intakes.

The mean serum cholesterol varied, but was mostly above normal reference ranges in both the experimental and control groups (KDIGO, 2013). Although it is clear and documented in many guidelines that CRF is associated with an increase in CVD risk, it is still not included in many assessment tools as there is also a lack of ethnicity and regional specific tools available (KDIGO, 2013). The under prescription/ under utilization of cholesterol lowering drugs could have been highlighted in this population group had there been a specific assessment tool for CVD risk.

Most of the participants had inadequate energy, protein, carbohydrate and fat intakes according to the recommended reference ranges (KDOQI, 2006). The information obtained by the patients in the 24-hour recall could, however, have been over- or underreported. The researcher used the (MRC) Food Flash Cards and Food Photo Manual in establishing correct portion sizes and cooking methods. The MRC Food Quantities Manual (Langenhoven et al., 1991) was used to convert reported food intake into household measures to be analysed using Foodfinder 3 (2003). This software has certain limitations that the researcher was aware of; however, it is the only software available that uses the MRC Food Composition database developed on South African foods and recommended for research purposes in SA. The dietary behaviour and nutrition knowledge was not an aim or objective of this trial, but could have provided more insight more reasons of lower dietary energy intake.

Wilson *et al.* (2006) raised an important factor of food security that needs to be added to the nutritional assessment of patients receiving dialysis. Patients receiving hemodialysis treatment need to be checked for possible food insecurity in order for appropriate intervention to be planned and carried out by renal health care professionals (Wilson *et al.,* 2006). The control group received no protein supplementation, which was the standard practice of care at Frere Hospital at the time of the trial from September to December 2012. The trial was not blinded due to the nature of the study. Therefore, food insecurity played a big role in this, particularly in the experimental group, who replaced their dietary intake with the protein powder supplements. The results can be seen in the dietary food records, where the experimental group's total dietary intake and macronutrient intake decreased during the intervention period as they were aware that the supplement they were receiving was a protein powder supplement, and cut back on expensive dietary protein. Literature shows that SA, and especially the EC province has a large prevalence of malnutrition due to food insecurity and low employment rates; which was seen in this trial. This is an important consideration when one decides to invest money to support patients receiving CAPD with a protein supplement.

The dietary intakes show that the participants in the experimental group had lower energy and fat intakes in the second month of the intervention as they were already ingesting the protein powder. This result could have been attributed to the extra protein ingestion through the protein powder as protein has a satiety effect on participants. The dietary fat intakes of participants were also not controlled or standardised and would be almost impossible to standardise in this study or future studies.

The researcher could not control the participant compliance to adding the protein powder to their meals; however the compliance was generally very good and better than other supplementation studies. (Aguirre-Galindo *et al*., 2003; Eustace *et al*., 2000; Heaf *et al.* 1999; Jeloka *et al.,* 2013; Kalantar-Zadeh *et al*., 2011; Teixidó-Planas *et al*, 2005). The reasons for noncompliance to protein supplements in this study were too general and should have been more specific like Jeloka *et al.* (2013), who found a higher prevalence of intolerance to protein supplements due to bloating, nausea, vomiting and anorexia.

Chapter 6: Conclusions and recommendations

6.1 Introduction

In this trial the socio-demographic profile and nutritional status of the study population receiving CAPD at Frere Hospital in East London were determined and described at baseline. The study population was paired into an intervention (n=13) and a control (n=13) group. The intervention group was supplemented and followed over a four month period, after which the effect of the supplementation on the nutritional status was assessed. The conclusions and recommendations based on findings are summarised in this chapter.

6.2 Conclusions

This is the first study to describe the patient population treated by CAPD at Frere Hospital, EC, SA. The general profile can be summarised as follows:

6.2.1 The profile of the patient population receiving CAPD at Frere Hospital, EC, SA

6.2.1.1 Socio-demographic and medical profile

This trial recruited 26 of the 28 patients receiving CAPD at Frere Hospital in 2012. Participants were 76% female and 80% Black, although the incidence of ESRD is generally higher among males than females, according to literature (Naicker, 2002; Coresh *et al.,* 2007; Schrier, 2009; Abdu *et al.,* 2011). The median age of participants was relatively young at 39.8 years in the experimental group (25 to 54 years old) and 37.2 years in the control group, which is similar to the findings of the only other three South African studies to date (Isla *et al.,* 2014*;* Abdu *et al.,* 2011; Naicker, 2002). Overall 84% were unemployed and relied on grants as their main source of income. Hypertension was the main cause of renal failure, and main co-morbidity, in 80% and 92%, respectively, which is consistent with literature on patients with CRF. Only a third of participants in both groups lived closer than 50km from the dialysis unit, while 15% in the experimental group and 25% in the control group lived more than 201km away. Overall 84% lived farther than 50 km away for Frere Hospital. If not for CAPD, patients living this far from a major centre, would not normally have access to RRT. In contrast to other SA studies, the duration that the participants had been receiving CAPD was relatively short.

6.2.1.2 Anthropometry measurements

Unlike international studies, but similar to other South African studies, BMI and AMA measurements in the higher than normal ranges, were reported in both groups. At baseline none were underweight, based on BMI; rather 35% were overweight/obese. Based on upper arm muscle area (AMA) none were wasted. Peritoneal solutions contain glucose, which is absorbed by the patients through the peritoneal membrane on a daily basis and therefore these patients initially gain weight in the first 12 to 18 months (Schrier, 2009). The duration of CAPD in this trial (medians of five to eight months in the experimental and control groups, respectively) was still within this time span of when patients usually gain weight. Weight loss may still follow later in their treatment. The high prevalence of overweight/obesity among the participants receiving CAPD at Frere Hospital, however, also reflects BMI among the general South African population as reported recently (Shisana *et* al, 2013).

6.2.1.3 SGA nutrition assessment tool

SGA nutrition assessment tool identified 23% as mildly to moderately malnourished, and only one participant as severely malnourished. These findings were consistent with studies done in North American, European and Korean participants (Young *et al*., 1991; Chung *et al*., 1999), but differ from that of South African and Indian studies who found more patients to be malnourished based on SGA nutrition assessment tool (Naiker, 2002; Abdu *et al.,* 2011).

6.2.1.4 Biochemistry measures

Despite the anthropometry suggesting better nutritional status among these participants than what is generally reported for patients receiving CAPD in international studies, serum albumin and sodium levels were generally low, which could be related to the high prevalence of edema or overhydration present in the study population. Almost half the participants had above normal serum phosphate levels which may reflect poor compliance to dietary guidelines for phosphate restriction, or failure to use phosphate binders with each meal or snack. All of the participants in the trial had an above normal serum urea and serum creatinine, which is consistent with ESRD (Abdu *et al.,* 2011), but should be controlled by dialysis. Only two participants in the experimental group received adequate dialysis in terms of the Kt/V formula. None of the participants in the trial received adequate dialysis when comparing the creatinine clearance. The cause of the overall inadequate dialysis needs to be further investigated and addressed.

6.2.1.5 Dietary intake

Compared to the KDOQI (2006) recommendations, most participants had inadequate intakes of energy (72%), protein (56%), HBV protein (64%), carbohydrate (52%) and fat (60%). The energy intakes and macronutrient distribution was therefore inadequate for most participants in the two groups, despite that the majority of the participants in both groups had a normal BMI, normal AMA and were classified as well-nourished according to the SGA nutrition assessment tool tool. Under reporting of dietary intake may be a possible explanation. The overall inadequate dialysis, reflected in the highly elevated serum levels of waste products in this study population, may also have contributed to poor appetite in both groups.

6.2.2 The effect of protein supplementation on the nutritional status of the study population

The effect of supplementing the intervention group with 0.65g/kg of a commercially available protein powder (*Protifar, Nutricia*), on nutritional status is summarised as follows.

6.2.2.1 Anthropometry measurements

Positive tendencies were shown in anthropometry measurements for the experimental groups when comparing the change from baseline to post-intervention, although these results were not statistically significant. Protein powder supplementation may positively influence various parameters of nutritional status, such as an increased BMI and an increased AMA. There was a tendency for the control group to lose weight, but this was not statistically significant (95% CI for the percentage difference [-40.7%; 18.3%]).

6.2.2.2 SGA nutrition assessment tool

Positive tendencies were seen in SGA nutrition assessment tool scores of the experimental group, as participants generally achieved a higher SGA nutrition assessment tool score at the end of the trial, compared to the control group (95% CI [-43.9%; 17.1%]).

6.2.2.3 Biochemistry measures

A statistical significant difference between the groups at month two for variable serum potassium and serum sodium was recorded. A statistical difference was also found between the two groups for edema present in month three and could explain the statistical significance for the lower serum sodium as the edema/ an increased fluid status decreases the serum sodium concentrations (Arroyo, 2008).

A low serum albumin is the strongest predictor of mortality in CRF participants (Beddhu *et al*., 2002; Lacson *et al., 2009*). A positive tendency towards an increase in serum albumin from baseline to post-intervention, was reported in the experimental group**.** Though not statistically significant, this may indicate some clinical benefit.

6.2.2.4 Dietary intake

While there was no statistical significant differences between the two groups regarding energy and macronutrient intakes at baseline and after the first month, at the end of the second month energy intakes and fat intakes were significantly higher in the control than in the experimental group. Protein powder supplements have been reported to decrease appetite and cause gastrointestinal discomfort. Furthermore, this trial was open-label and the experimental group was aware that they were receiving a protein powder supplement. It is possible, given the poor socio-economic status of this study population that they could have cut back on their intake of protein-rich foods, which are generally expensive.

6.2.2.5 Protein supplementation and compliance

The compliance to using the protein powder was generally good at more than 82% throughout the trial. The best compliance was reported during the last month, while the worst compliance was reported during the second month of the trial. Further research is needed regarding the factors that predict adherence to dietary prescriptions among South African populations.

6.2.2.6 Summary

Although protein supplementation did not have a statistically significant impact on the nutritional status of CAPD patients in this trial, some non-significant improvements in anthropometry measurements, SGA nutrition assessment tool score and albumin status, suggest that studies of larger size with supplementation over a longer period of time may achieve more positive results.

6.2.3 Summary of the limitations of the current trial

The limitations of the current trial are summarised below from the baseline assessment, intervention period and post-intervention.

i. This sample of participants only represented the patients from East London and surrounding areas who received CAPD of Frere Hospital. Not all patients receiving CAPD in the EC region were used due to logistical and time constraints.

ii. A small sample size of the population could have affected the results; however almost the whole population of patients receiving CAPD at Frere Hospital were included. These low numbers reflects the low number of patients with CRF in SA on RRT that receive CAPD (Abu-Aisha & Elamin, 2009). Other clinical trials in the population receiving CAPD tend to also have small sample sizes (Abdu *et al.,* 2011).

iii. The researcher could not control the number of participants lost in the trial due to CAPD being stopped (death or medical practitioner's decision to stop CAPD). One participant in the control group died before the intervention trial started; one participant in the experimental group changed from CAPD to HD during the intervention, and one participant in the control group had transport issues during transport strikes in the EC region over December 2012, preventing him from coming to the CAPD dialysis unit. Both these participants were thus excluded from the final follow-up assessment.

iv. The situation at work, and facilities available for participants who had part time or full time employment was not assessed in this trial; but could have provided valuable insights into factors that influence compliance to dialysis, medication and dietary advice.

v. Factors which may shorten the duration of CAPD and cause switching to HD, is poor fluid and volume control, as well as the occurrence of peritonitis, which is especially seen in the first 12 – 24 months of initiating CAPD (Chaudhary, 2011). These factors were not assessed in the current trial and may have shed light on the short median duration of CAPD in this trial population, as well as their electrolyte profiles.

vi. BMI is not specific for the ESRD population and thus the BMI was compared to the standard values for a general population according to KDIGO (2013); there is a need for more specific BMI reference ranges for patients with ESRD. It would be interesting to repeat this study in the same sample of participants, as weight gain is typically experienced during the 12-18 months following the initiation of CAPD, due to the absorption of glucose through the peritoneal membrane on a daily (Schrier, 2009).

vii. Low serum albumin levels are associated with high mortality rates (Fouque, 2007; Kopple, 1994). More than 60% of this study population had a serum albumin of less than 30g/L. Serum albumin levels however also decrease in response to inflammation, as it is a negative acute phase reactant. This may have been a source of bias in the trial.

CRP measurement, which as a positive acute phase reactant, may be used as a marker of inflammation, was not obtained in this trial due to lack of resources in the hospital (Kalantar-Zadeh *et al*., 2011).

viii. A statistical significant difference was noted between the two groups during month two for serum potassium, where the serum potassium was significantly higher in the control than in the experimental group. The reason for this difference could be due to a higher dietary potassium intake, but this was not an objective of the trial. The dietary intake parameters measured did not include electrolyte intakes, but rather focused on energy, protein, carbohydrate and fat intake. Serum phosphate levels were elevated in half of the experimental group and two thirds of the control group at post-intervention; which could be due to a higher phosphate intake (meat and/or protein powder supplementation) or non compliance to phosphate binder medication.This trial should have also included and analyzed the dietary potassium, phosphate and sodium intakes.

ix. The serum cholesterol measurements beyond month two was not determined in the trial due to limited funding at the hospital. The median serum cholesterol levels varied, but were mostly above normal reference ranges in both the experimental and control groups (KDIGO, 2013). Although it is clear and documented in many guidelines that CRF is associated with an increase in CVD risk, it is still not included in many assessment tools as there is also a lack of ethnicity and regional specific tools available (KDIGO, 2013). The under prescription/ under utilization of cholesterol lowering drugs could have been highlighted in this population group had there been a specific assessment tool for CVD risk.

x. Most of the participants had inadequate energy, protein, carbohydrate and fat intakes according to the recommended reference ranges (KDOQI, 2006). The information obtained by the patients in the 24-hour recall could have been over or underreported. The researcher used the (MRC) Food Flash Cards and Food Photo Manual in establishing correct portion sizes and cooking methods. The MRC Food Quantities Manual (Langenhoven et al., 1991) was used to convert reported food intake into household measures to be analysed using Foodfinder 3 (2003). This software has certain limitations that the researcher was aware of; however, it is the only software available that uses the MRC Food Composition database developed on South African foods and recommended for research purposes in SA.

The dietary behaviour and nutrition knowledge was not an aim or objective of this trial, but could have provided more insight more reasons of lower dietary energy intake.

xi. There is some possibility that given the socio-economic status of this study population, the experimental group may have cut back on their intake of protein-rich foods, which are generally expensive. Wilson *et al.* (2006) raised an important factor of food security that needs to be added to the nutritional assessment of patients receiving dialysis. Literature shows that SA, and especially the EC province, has a high prevalence of malnutrition due to food insecurity and low employment rates. This is an important consideration before money is invested in supplements to support patients receiving CAPD. The control group also did not receive any placebo powder, but rather received the standard care, which was no powder which may have influenced this result.

xii. The dietary intakes show that the participants in the experimental group had lower energy and fat intakes in the second month of the intervention compared to the control group. This result could have been attributed to the protein powder which may have a satiety effect. Standardising macronutrient intakes would have been impossible. Dietary data measurements beyond month two was not collected due to time constraints, as the other data took longer than anticipated to collect.

xiii. Reported compliance to adding the protein powder to meals were generally very good and better than other supplementation studies (Aguirre-Galindo *et al*., 2003; Eustace *et al*., 2000; Heaf *et al.* 1999; Jeloka *et al.,* 2013; Kalantar-Zadeh *et al*., 2011; Teixidó-Planas *et al*, 2005). There is, however, no way to establish if participanst were indeed truthful on this matter.

xiv. Some results for anthropometry, SGA nutrition assessment tool scores, biochemical measures and adequacy of dialysis were missing during the trial due to a number of factors. Ongoing transport strikes in the area of the study prevented a few of the participants from coming to the hospital, and the researcher and the nurses were not able to go to the participant's houses due to the long distance and lack of resources to perform the tests away from the hospital. Insufficient time prevented the researcher from repeating the tests before the patients' next follow up at the hospital, as data was collected on monthly points. Some participants also forgot or were not physically able to come on their certain day and thus came one or two weeks before or after their planned date (which was spaced out evenly within the data collection period).

xv. Bias from the researcher could have resulted in this trial, as the researcher was not blinded to who received the protein supplements and the SGA nutrition assessment tool tool is a subjective measure, that was conducted by the researcher.

6.3 Recommendations

Based on these conclusions, the following recommendations are made:

6.3.1 Recommendations for policy

i. With the large prevalence of patients with ESRD, work places and employers need to be able to accommodate patients receiving CAPD. Guidelines need to be set up so that the employer knows what facilities are needed for these patients, such as a suitable room to do the exchanges, hygienic facilities, as well as sufficient storage space; which is a barrier for participants receiving CAPD being employed.

ii. BMI is not specific to the ESRD population and thus the BMI is compared to the standard values for a general population according to KDIGO (2013); there is a need for more specific BMI reference ranges for patients with ESRD in a South African setting.

6.3.2 Recommendations for practice

i. Patients with renal failure should be referred to a nephrologist early enough so that timeous and efficient treatment, with efficient monitoring of among others, the biochemical parameters, may be implemented. This may make a possible kidney transplant feasible for more patients, ensuring that CAPD may be a short, rather than long term solution.

ii. Patients should be referred to the dietitian early. Dietitians play an integral role in interpreting the contextual nutritional status of the patient, which also includes obtaining a complete diet and lifestyle history from the patient; on the basis of which thorough and individualised counselling can be done.

iii. All nurses at a primary health care level should be trained to accurately measure and screen patient's blood pressure and blood glucose as poorly controlled diabetes leads to excessive thirst and thus the patient will consume more fluids and further negatively impact edema. Poorly controlled blood pressure further places a strain on the kidneys and is a factor which can shorten the duration of CAPD (and switching to HD) due to poor fluid and volume control.

iv. It is vitally important to monitor patient's compliance to medication, such as cholesterol lowering medication and phosphate binders. Although the mean serum cholesterol varied in this trial, it was mostly above normal reference ranges in both the experimental and control groups and could indicate non-compliance to medication (KDIGO, 2013). The serum phosphate was also poorly controlled in this trial and could indicate non-compliance to phosphate binders.

6.3.3 Recommendations for health care professionals

i. Health care professionals need to stay up to date with the latest scientific information regarding the benefits of CAPD, which is a cheaper modality of RRT than of HD and can then help the patients make an informed decision regarding treatment options.

ii. Regular check-ups should be arranged with the nephrologist, to ensure that patients are receiving adequate dialysis. Specifically Kt/V should be assessed and interpreted, as there were almost no participants in the current trial who received adequate dialysis. This is also recommended by major international practice guidelines, as underdialysis contributes to PEW (KDOQI, 2006).

iii. Periodic assessment of nutritional status of all patients with CRF, should form part of routine care for early detection and management of malnutrition and wasting. A registered dietitian should be in charge of these proceedings, and should stay abreast of, and be trained in the use of the most effective evidence-based tools for screening for malnutrition in this population (BMI, AMA, SGA nutrition assessment tool, dietary intake).

iv. Health care professionals at a primary health care level need to accurately screen and measure patients' blood pressure and blood glucose levels to ensure the prevention of CRF; as well as to improve the clinical outcomes in patients with ESRD.

v. The under prescription/ under-utilization of cholesterol lowering drugs and phosphate binders were not an outcome in this trial, but could have been highlighted in this population group and it is the health care professionals' responsibility to ensure patients understand the implications of non-compliance to medication on their long term health.

6.3.4 Recommendations for future research

i. Future studies, especially clinical trials, to assess the effect of nutrient supplementation in patients receiving CAPD, should include larger sample sizes, in order to improve the statistical power of the results. This may be a challenge, as the current trial, including 26 participants, included the whole population receiving CAPD in the BC district of the EC.

ii. Future clinical supplementation trials in the CAPD population should be double-blinded and placebo-controlled. In the current trial, participants knew they were receiving protein powder supplementation which seen to have caused them to cut back on protein rich food which is expensive.

iii. The populations of patients receiving CAPD in other areas of SA, should also be profiled, as information, following the current trial, is only available for the BC district of the EC, and the Johannesburg, Durban and Limpopo areas.

iv. The current trial should be repeated in the near future in the same participants, as the literature reports that weight loss and wasting is usually experienced after 12-18 months of initiating CAPD (Schrier, 2009). The median duration of CAPD was relatively short in the current study population.

v. The dietary behaviour and nutrition knowledge of patients receiving CAPD should be studied to provide more insight into the causes of inadequate dietary intakes in this population in the unique South African context. South African studies show that there is a lack of health and nutrition knowledge in the general population, despite an improved level of education in the past few years (Steyn *et al.,* 2000; Kruger *et al.,* 2002; Mchiza, 2008, SANHANES-1, 2012). Future studies should also include and analyze the dietary potassium, phosphate and sodium intakes; which is relevant to patient care in this population.

vi. The findings of the current trial should be compared to similar parameters among patients receiving CAPD in private health care to determine if the same challenges are found in state institutions and private institutions. Even though the majority of participants in this trial who received protein powder supplementation, did not lose weight, there was a tendency for the control group to lose weight and therefore solutions to the problem of malnutrition in patients need to be identified. There was a statistically significant difference between the two groups in this trial when comparing income, and more participants in the experimental group were unemployed or received no income. Wilson *et al.* (2006) raised an important factor of food security that needs to be added to the nutritional assessment of patients receiving dialysis.

vii. A study similar to the current trial should be performed on the patients receiving HD at Frere Hospital, to allow further conclusions to be made about the patients receiving HD living in the same area as such a study in this area has not been performed to date.

viii. Due to the short mean duration of participants receiving CAPD, more research is need regarding the quality of life in patients with ESRD in the South African population. The impact of treatment modality on social relationships and psychological adjustment, which has an effect on employment aspects as well as the duration in which patients stay on a certain modality, should be explored in the South African context (Griffin *et al.,* n.d).

ix. The working situation and facilities available for participants within the workplace needs to be explored and described in South African studies, as to provide insight into the work place and whether there is a room to do the exchange, as well as sufficient storage space; which is a big barrier for participants receiving CAPD being employed.

x. More research regarding the adequacy of dialysis (dialysis success) should be investigated in patients receiving dialysis in SA. Underdialysis was highlighted in this trial and studies suggest it leads to malnutrition.

6.3.5 Summary of recommendations

This is the first trial to describe the socio-demographic and nutritional status profile of patients receiving CAPD in the EC. A similar socio-demographic profile as described in other studies for the South African CAPD population in Johannesburg, Durban and Polokwane, was found (Isla *et al.,* 2014*;* Abdu *et al.,* 2011; Naicker, 2002). The anthropometric profile was however found to be very different to that described for CAPD patients in developed countries, with a high prevalence of overweight/obesity. The causes of the overall inadequate dialysis reflected in highly elevated serum levels of waste products in this study population, needs to be investigate further. Although protein supplementation did not have a statistically significant impact on the nutritional status of CAPD patients in this trial, some non-significant improvements in anthropometry and biochemical indicators, suggest that studies of larger size with supplementation over a longer period of time are needed.

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8 Appendices

A Randomised Controlled Clinical Trial of Protein supplementation on the nutritional status in patients receiving CAPD in Frere Hospital, East London

Appendix 1

Socio-demographic Information

1. Subject number _____
2. Group _____
3. Date _____

4. Age _____ years

5. Date of Birth _____

6. Gender _____

1	Male
2	Female

7. Race _____

1	Black
2	Coloured
3	Indian
4	White

8. Distance from patient's home to CAPD clinic

1	< 50 kilometers
2	51-100 kilometers
3	101-200 kilometers
4	>201 kilometers

9. How many people live in your house?_____

10. Are you employed? _____

1	No
2	Employed: Full time
3	Employed: Part time
4	Pensioner
5	Grant
6	Other _____

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Medical History

11. Aetiology of CRF _____

1	Hypertension
2	Diabetes Mellitus
3	Glomuruler Nephritis
4	TB
5	Other _____

12. Morbidities present _____

More than one option may be selected.

1	Hypertension
2	Diabetes Mellitus
3	Glomuruler Nephritis
4	TB
5	Anaemia
6	Renal osteotrophy
7	Other _____

Medications

	Medication	Dosage	Unit
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12	Other:		

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CAPD Regime

13. Duration of CAPD _____ months

14. Date when CAPD started _____

15. Type of CAPD solution _____
More than one option may be selected.

1	Dianeal (1.5%)
2	Dianeal (2.5%)
3	Dianeal (4.25%)
4	Extraneal
5	Nutrineal
6	Physioneal

16. Number of daily exchanges _____

1	One
2	Two
3	Three
4	Four
5	Five
6	Six
7	More than six

17. Presence of temporary HD line_____

1	Yes
2	No

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Appendix 2

Anthropometry Measurements

Measurements are rounded off to one demimal point.
Three measurements need to be taken for point 9 and 10.

1. Subject number _____
2. Group _____
3. Date _____

4. Weight _____._____ kg

5. Edema present

1	Yes _____._____ kg
2	No

6. Dry weight _____._____ kg

7. Height _____ cm

8. BMI _____._____ kg/m^2

9. MUAC

1	_____ mm
2	_____ mm
3	_____ mm

10. TSF

1	_____ mm
2	_____ mm
3	_____ mm

11. AMA _____ mm^2

$$AMA\ (mm^2) = \frac{(MUAC - \pi\ TSF)^2}{4\ \pi}$$

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Appendix3

Subjective Global Assessment

1. Subject number _____
2. Group _____
3. Date _____

Score according to the 7 Point Lickert Scale:

	Rating
1	Very severe
2	Severe
3	Moderate - severe
4	Moderate
5	Mild – moderate
6	Mild
7	None

A. History

1. Weight changes

1.1 Over the past 2 weeks

1	2	3	4	5	6	7	
							Increasing weight
							Stable weight
							Ongoing weight loss

1.2. Weight changes over the past 6 months

1	2	3	4	5	6	7	
							< 5% weight change (or gain)
							5 – 10% weight loss
							>10 % weight loss

2. Food intake:

2.1 Overall

1	2	3	4	5	6	7	
							Usual intake
							< Usual intake & decreasing

2.2 Duration of <usual intake _____ weeks

1	2	3	4	5	6	7	
							< Usual intake

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2.3 Type of change

1	2	3	4	5	6	7	
							Suboptimal solids
							Full liquid intake
							Hypocaloric fluids
							Unable to eat

B. Physical Examination

1. Loss of subcutaneous fat

1	2	3	4	5	6	7	
							Below eyes
							Triceps
							Biceps
							Chest

2. Muscle wasting

1	2	3	4	5	6	7	
							Temple
							Clavicle
							Scapula
							Ribs
							Quadriceps
							Calf
							Knee
							Interosseous

3. Edema present

1	2	3	4	5	6	7	
							Hand
							Sacrum
							Feet

C. Overall SGA Classification

1	Normal to well nourished (6 or 7 ratings)
2	Mild to moderately malnourished (3,4,5 ratings)
3	Severely malnourished (1 or 2 ratings)

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Appendix 4

Biochemistry Investigations

1. Subject number _____
2. Group _____
3. Date _____

4. Serum albumin _____ g/L
5. Serum sodium _____ mmol/L
6. Serum potassium _____._____ mmol/L
7. Serum phosphate _____._____ mmol/L
8. Serum urea _____._____ mmol/L
9. Serum creatinine _____ umol/L
10. Serum cholesterol _____ mmol/L
11. CRP _____ mg/L

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Appendix 5

Dietary intake
24-hour Recall

1. Subject number _____
2. Group _____
3. Date _____
4. Food Record _____

Time	Food item	Portion Size	Cooking Method

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Appendix 5

Evaluation of dietary intake:

1. Subject number _____
2. Group _____
3. Date _____
4. Food Record _____

5. Energy (kJ) _____

6. Carbohydrate (g) _____

7. Protein – Total (g) _____

8. Protein – High Biological Value (g) _____

9. Fat (g) _____

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Appendix 6

1. Subject number _____

2. Group _____
3. Date _____

Instructions:

1. Fill out the block, with a tick (√) under "yes" or "no" if you put the protein powder in your food/drink for each day.
2. If you did not add the powder to your food or drink, please give a reason for this in the block.
3. Be as honest as possible.

Day	Date	Yes	No	Reason why didn't add powder
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
Day 6				
Day 7				
Day 8				
Day 9				
Day 10				
Day 11				
Day 12				
Day 13				
Day 14				

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Appendix 6

1. Subject number _____

2. Group _____
3. Date _____

Day	Date	Yes	No	Reason why didn't add powder
Day 15				
Day 16				
Day 17				
Day 18				
Day 19				
Day 20				
Day 21				
Day 22				
Day 23				
Day 24				
Day 25				
Day 26				
Day 27				
Day 28				
Day 29				
Day 30				
Day 31				

Evaluation of protein powder intake

4. Number of days: intake _____

5. Number of days : missed intake _____

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Appendix 7

Deelnemer nommer _____

2. Groep _____
3. Datum _____

Instruksies:

1. Vul die blokkies uit, met 'n kruis onder "ja" of "nee" vir elke dag wat u die poeier in u kos/drank gesit het.
2. As u nie die poeier in u kos/drank ingesit het nie, verskaf asseblief redes in die blokkie daarvoor aangedui.
3. Antwoord asseblief so eerlik as moontlik.

Dag	Datum	Ja	Nee	Rede waarom poeier nie gebruik is nie
Dag 1				
Dag 2				
Dag 3				
Dag 4				
Dag 5				
Dag 6				
Dag 7				
Dag 8				
Dag 9				
Dag 10				
Dag 11				
Dag 12				
Dag 13				
Dag 14				

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Appendix7

1. Deelnemer nommer _____

2. Groep _____
3. Datum _____

Dag	Datum	Ja	Nee	Rede waarom poeier nie gebruik is nie
Dag 15				
Dag 16				
Dag 17				
Dag 18				
Dag 19				
Dag 20				
Dag 21				
Dag 22				
Dag 23				
Dag 24				
Dag 25				
Dag 26				
Dag 27				
Dag 28				
Dag 29				
Dag 30				
Dag 31				

For official use: Evaluation of protein powder intake

4. Number of days: taken powder _____

5. Number of days : missed powder _____

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Appendix 8

1. Inombolo _____
2. Iqela _____
3. Umhla _____

Imiqathango:

1. Gcwalisa ibhokisi, ngokuthi utikishe (√) ngaphantsi “ewe” okanye “hayi” ukuba uyawugalela umgubo weproteni ekutyeni/kwisiselo sakho.
2. Ukuba akuwugaleli umgubo ekutyeni okanye kwisiselo sakho, nceda nika isizathu soko ebhokisini.
3. Uzuncede unyaniseke kangangoko.

Usuku	Umhla(date)	Ewe	Hayi	Isizathu sokungawugaleli umgubo
Usuku 1				
Usuku 2				
Usuku 3				
Usuku 4				
Usuku 5				
Usuku 6				
Usuku 7				
Usuku 8				
Usuku 9				
Usuku 10				
Usuku 11				
Usuku 12				
Usuku 13				
Usuku 14				

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Appendix 8

1. Inombolo _____
2. Iqela _____
3. Umhla _____

Usuku	Umhla(date)	Ewe	Hayi	Isizathu sokungawugaleli umgubo
Usuku 15				
Usuku 16				
Usuku 17				
Usuku 18				
Usuku 19				
Usuku 20				
Usuku 21				
Usuku 22				
Usuku 23				
Usuku 24				
Usuku 25				
Usuku 26				
Usuku 27				
Usuku 28				
Usuku 29				
Usuku 30				
Usuku 31				

For official use: Evaluation of protein powder intake

4. Number of days: taken powder _____

5. Number of days : missed powder _____

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Appendix 9

Dialysis Adequacy

Measurements are rounded off to one demimal point.

1. Subject number _____
2. Group _____
3. Date _____

4. Transport Status _____

1	Slow Transporter
2	Medium Transporter
3	Fast Transporter

5. Weight _____._____kg
6. Height _____cm
7. Age _____years

8. Urine measurements
8.1 Urea _____mmol/L
8.2 Creatinine _____umol/L
8.3 Volume _____ ml

9. Dialysis measurements
9.1 Urea _____mmol/L
9.2 Creatinine _____umol/L
9.3 Volume _____ ml
9.4 Albumin lost _____ g

10. Blood measurements
10.1 Urea _____mmol/L
10.2 Creatinine _____umol/L

11. Weekly kt/v _____
12. Weekly Creatinine clearance _____

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CONSENT TO PARTICIPATE IN THE RESEARCH Appendix 10

1. Subject number _____
2. Group _____
3. Date _____

You have been kindly invited to participate in this study.

You have been informed about the study by Brigitte Leclercq, the dietician of Frere Hospital's Renal Unit; who is also a student at the University of the Free State (UFS).

Questions regarding the study may be directed to the researcher, Ms Leclercq at any time at the following numbers: 071 482 7437 or 043 709 2427.

You may contact the Secretariat of the Ethics Committee of the Faculty of Health Sciences, UFS at telephone number (051) 4052812 if you have questions about your rights as a research subject.

Your participation in this research is voluntary, and you will not be penalized or lose benefits if you refuse to participate or decide to terminate participation.

If you agree to participate, you will be given a signed copy of this document as well as the participant information sheet, which is a written summary of the research.

The research study, including the above information has been verbally described to me. I understand what my involvement in the study means and I voluntarily agree to participate.

_____ _____
Signature of Participant Date

_____ _____
Signature of Witness Date

_____ _____
Signature of Translator Date

A Randomised Controlled Clinical Trial of Protein supplementation on the nutritional status in patients receiving CAPD in Frere Hospital, East London

TOESTEMMING TOT DEELNAME AAN NAVORSING Appendix 11

1. Deelnemer nommer _____

2. Groep _____
3. Datum _____

U word vriendelik versoek om aan 'n navorsingstudie deel te neem.

Brigitte Leclercq het u oor die studie ingelig. Sy is die dieetkundige in Frere Hospitaal se Nier Saal en ook 'n student by die Universiteit van die Vrystaat (UVS).

Me Leclercq kan enige tyd gekontak word by 071 482 7437 of (043) 709 2427 indien u vrae oor die navorsing het of indien u as gevolg van die navorsing beseer is.

Die Sekreteriaat van die Etiekkomitee van die Fakulteit Gesondheidswetenskappe, UVS kan by (051) 4052812 gekontak word indien u enige vrae het oor u regte as 'n proefpersoon.

U deelname aan hierdie navorsing is vrywillig en u sal nie gepenaliseer word of voordele verbeur as u weier om deel te neem of besluit om deelname te staak nie.

As u instem om deel te neem, sal 'n ondertekende kopie van hierdie dokument sowel as die deelnemerinligtingsblad, wat 'n geskrewe opsomming van die navorsing is, aan u gegee word .

Die navorsingstudie, insluitend die bogenoemde inligting is verbaal aan my beskryf. Ek begryp wat my betrokkenheid by die studie beteken en ek stem vrywillig in om deel te neem.

_____ _____
Handtekening van deelnemer Datum

_____ _____
Handtekening van getuie Datum

_____ _____
Handtekening van vertaler Datum

A Randomised Controlled Clinical Trial of Protein supplementation on the nutritional status in patients receiving CAPD in Frere Hospital, East London

ILUNGELO LOKUBA YINXALENYE KUPHANDO Appendix 12

1. Inombolo _____
2. Iqela _____
3. Umhla _____

Uyamenywa sihlobo ukuba ubeyinxalenye yesisifundo.

Uzakuchazelwa ngesisifundo ngu Brigitte Leclercq, udietician we Frere Hospital's Renal Unit; oye wafunda kwi University of the Free State (UFS).

Imibuzo malunga nesisifundo ingathunyelwa ngqo kumphandi, uMs Leclercq nangaliphi ixesha kwezi nombolo zilandelayo: 071 482 7437 or 043 709 2427.

Ungahlangana no nobhala we Ethics Committee ye Faculty of Health Sciences,UFS uMs Strauss weUniversity of Free State kule nombolo (051) 4052812 ukuba unemibuzo mayelana nalungelo akho nje ngomntu esiphanga ngaye.

Ukuba yinxalenye kwakho kolu phando kukuzinikela, kwaye uwuyikohlwaywa okanye ulahlekelwe zizinto akuyala ukuba yinxalenye okanye ubenesigqibo sokuyeka phakathi.

Ukuba uyakwamkela ukuba yinxalenye, uzakunwa usayine a signed kwiphetshana elinenkcukacha nenkcazelo ngomthabathi nxaxheba,izakuba ibhalwe ngokufutshane ngophando.

Isifundo sophando,kwakunye nale nkcazelo ingentla seyichaziwe kum.Ndiyakuqonda kuthetha ntoni what uzibandakanya nesisifundo kunye nokuzinikezela kwam ukuba ndibe yinxalenye.

_____ _____
Signitsha yomthathi nxaxheba Umhla

_____ _____
Signitsha yengqina Umhla

_____ _____
Signitsha yomguquli ntetho Umhla

A Randomised Controlled Clinical Trial of Protein supplementation on the nutritional status in patients receiving CAPD in Frere Hospital, East London

INFORMATION DOCUMENT Appendix 13

1. Subject number _____
2. Group _____
3. Date _____

Dear Participant

Research: A Randomised Controlled Clinical Trial of Protein supplementation on the nutritional status in patients receiving CAPD in Frere Hospital, East London

I, Brigitte Leclercq, am doing research on the nutritional status and the importance of a healthy lifestyle in CAPD patients. Research is just the process to learn the answer to a question. In this study we want to learn more about your nutritional status and ways in which we can improve it.

I am inviting you to participate in a research study.

The Evaluation committee of the School of Allied professionals and the Ethics Committee of the Faculty of Health Sciences (ECUFS) have approved the study and its procedures. The procedures will not expose you to any physical or psychological harm. There is limited research available on the nutritional status of persons on continuous ambulatory peritoneal dialysis in South Africa. Your input will be of great value to the results of this study and for future advancement for other patients in dialysis.

This study is a randomised controlled clinical trial, in which you will be divided into two groups. This study will be conducted in the Renal Unit at Frere Hospital, and the information will be taken from your medical records. You need to come to the hospital for your monthly check ups and more information will be taken from you while at the hospital for your check ups. The procedure is explained below. All continuous ambulatory peritoneal dialysis (CAPD) patients at Frere Hospital will be included in the study, with a total number of 25 participants to be recruited at this site and altogether.

The procedure will include the following:

Routine follow up assessments will occur once a month, over the next three months, September-November 2012.

1. An interview during which questions on socio-demographic information, medical information, your CAPD Regime, dietary intake (by means of a 24-Hour Recall), weight changes and biochemistry results will be measured.
2. Body weight, height and skinfolds will be measured.
3. The normal three blood samples will be taken with a needle from you at your standard clinic visit.

4. The use of a protein powder if you are asked to take the powder (patients in group one), as indicated in the information session, by the dietician. One month supply will be given to you every month at your next routine follow up assessments.

There are no risks involved in taking part in this study. Participation in this study is voluntary and you have the right to withdraw at any time without any penalties. Normal patient care at the renal unit of Frere Hospital will continue. There is no compensation for participating in this study, but you will receive lunch for coming in for the assessments.

Efforts will be made to keep personal information confidential. Absolute confidentiality cannot be guaranteed. Personal information may be disclosed if required by law.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the Ethics Committee for Medical Research and the Medicines Control Council.

Results may be published or presented at a conference.

Questions regarding the study may be directed to the researcher, Ms Leclercq at any time at the following numbers: 071 482 7437 or 043 709 2427, or the secretariat of the Ethics Committee of the Faculty of Health Sciences, University of the Free State, Ms Strauss 051 4052812.

The research study, including the above information has been verbally described to me. I understand my involvement in the study and voluntarily agree to participate.

_____ _____
Signature of Participant Date

_____ _____
Signature of Witness Date

_____ _____
Signature of Translator Date

A Randomised Controlled Clinical Trial of Protein supplementation on the nutritional status in patients receiving CAPD in Frere Hospital, East London

INLIGTINGSDOKUMENT Appendix 14

1. Deelnemer nommer _____

2. Groep _____
3. Datum _____

Geagte Deelnemer

Navorsing: A Randomised Controlled Clinical Trial of Protein supplementation on the nutritional status in patients receiving CAPD in Frere Hospital, East London

Ek, Brigitte Leclercq, is besig om navorsing oor die voedingstatus en die belangrikheid van ‘n gesonde leefstyl in CAPD pasiënte te doen. Navorsing is slegs die proses waardeur die antwoord op ‘n vraagstuk verkry word. In hierdie studie wil ons meer leer oor u voedingsatus en manier waarop ons dit kan verbeter.

Ek nooi u uit om aan ‘n navorsingstudie deel te neem

Die Evaluasie Komitee van die Skool van Aanvullende Gesondheids Professionele Persone en die Etiese Komitee van die Fakulteit van Gesondheidswetenskappe het toestemming gegee dat die studie en die prosedure mag voortgaan. Die prosedure sal geen fisiese- of psigososiale skade doen nie. Daar is min navorsing in Suid Afrika oor die voedingsvlakke in mense wat op voortdurende ambulatoriese peritoneale dialise is. U insette sal baie beteken vir hierdie studie en toekomstige navorsing oor ander pasiënte op dialise.

Hierdie studie is ‘n lukrake gekontrolleerde kliniese proefneming en u sal in twee groepe ingedeel word. Die studie sal in die Nier Saal in Frere Hospitaal plaasvind en die inligting sal uit u mediese rekords kom. U moet maandeliks vir u opvolg evaluasies kom en nog inligting sal dan gemeet word. Die prosedure word onder beskryf. Al die voordurende ambulatoriese peritoneale dialise (CAPD) pasiënte by Frere Hospitaal sa ingesluit word, met ‘n totaal van 25 pasiënte wat hier en altesaam gewerf is.

Die prosedure sal die volgende insluit:

Roetine opvolg evaluasies sal een keer ‘n maand gebeur, oor die volgende drie maande, September-November 2012.

1. ‘n Onderhoud, met vrae wat sosio-demografiese inligting, mediese inligting, u CAPD regime, dieetkundige inname (by wyse van ‘n 24-uur herroeping), gewigsveranderinge en biochemiese resultate meet, sal gedoen word.

2. Liggaamsgewig, lengte en velvoue sal gemeet word.

3. Die drie normale bloed monsters sal geneem word by die standaard kliniek besoek.
4. Die gebruik van ‘n proteïenpoeier as u gevra is om die poeier te neem (pasiente in groep een), sal in die inligtingsessie gegee word, deur die dieetkundige. Een maand se voorraad sal maandeliks gegee word by u volgende roetine opvolg evaluasies.

Daar is geen risiko's om aan die studie deel te neem nie. Deelname aan die studie is vrywillig en u het die reg om enige tyd te onttrek, sonder dat u gepenaliseer gaan word. Normale pasiëntsorg by die Nier Saal in Frere Hospitaal gaan voortgaan. Daar is geen vergoeding om aan hierdie studie deel te neem nie, maar u sal middagete kry wanneer u vir die opvolg evaluasies kom.

Daar sal gepoog word om persoonlike inligting vertroulik te hou. Volkome vertroulikheid kan nie gewaarborg word nie.

Resultate kan by 'n konferensie gepubliseer of voorgedra word.

Organisasies wat u navorsingsrekords mag ondersoek en/of kopieer vir kwaliteitsversekering en data-analise sluit groepe soos die Etiekkomitee vir Mediese Navorsing en die Medisynebeheerraad in.

Vir verdere inligting/rapportering van studieverwante newe-effekte, kontak die navorser, Me Leclercq direk by die volgende kontaknommers: 071 482 7437 of (043) 709 2427; of die sekreteriaat van die Etiese Komitee van die Fakulteit van GesondheidsWetenskappe, Universiteit van die Vrystaat, Me Strauss by (051) 4052812.

Die navorsingstudie, insluitend die bogenoemde inligting is verbaal aan my beskryf. Ek begryp wat my betrokkenheid by die studie beteken en ek stem vrywillig in om deel te neem.

_____	_____
Handtekening van deelnemer	Datum
_____	_____
Handtekening van getuie	Datum
_____	_____
Handtekening van vertaler	Datum

A Randomised Controlled Clinical Trial of Protein supplementation on the nutritional status in patients receiving CAPD in Frere Hospital, East London

UKUCHAZWA KWENKCUKACHA Appendix 15

1. Inombolo _____
2. Iqela _____
3. Umhla _____

Mthathi nxaxheba othandekayo

Research: A Randomised Controlled Clinical Trial of Protein supplementation on the nutritional status in patients receiving CAPD in Frere Hospital, East London

Mna, Brigitte Leclercq, ndenza uphando kwinqanaba lwesondlo kunye nokubaluleka kwimpilo yobomi esibuphilayo sizizigulana eziDalayizwayo. Uphando yinkqubo yokufunda ngempendulo kumbuzo. Kwesisifundo sifuna ukufunda ngakumbi mayelana nendlela othi wondleke ngayo kunye nendlela esina ukuyiphuchula ngayo lonto.

Ndiyakumema ubeyinxalenye kwesisifundo sophando.

Ikomiti yophengululo ye School of Allied professionals kunye ne Ethics Committee of the Faculty of Health Sciences (ECUFS) basamkele esisifundo kunye nemigaqo yaso. Imigaqo engazukulimaza ngokwamzimbeni nangokwa sengqondweni. Kukho uphando olulinganiselweyo kwinqanaba lwesondlo somntu oluqhubekayo Ekudalayizweni eMzantsi Afrika. Igalelo lakho lizobaluleka kakhulu kwiziphumo zesisifundo kunye nakwixesha elizayo kwizigulana ezidalayiwzayo.

Esi sifundo is a randomised controlled clinical trial, ngako oko nizakohlulwa nibe ngamaqela amabini. Esi sifundo sizoqhutyelwa eRenal Unit at Frere Hospital, kunye nenkcukacha zizothatyatwha kwingxelo yakho yonyango. Kufuneka uze kuhlolo lwakho lweenyanga kunye nezinye inkcukacha zakho ngelixa usesibhedlele kuhlolo. Umgaqo uchaziwe ngezantsi. Bonke abaqhubekekayo dayalisis (umtshini ococa igazi osetyenziswa xa izintso zisohluleka) (CAPD) abazizigulana eFrere Hospital bazo bandakanywa kwesisifundo, kunye nenani eliqingqiweyo 25 yabathathi nxaxheba abazabhaliswa kwisibhedlele sonke.

Umgaqo uzakubandakanya oku kulandelayo:

Indlela ezakundela uvavanyo oluzabakho kanye ngenyanga, kangange nyanga ezintathu ezizyo, September- November 2012.

1. Udliwanondlebe ngexesha lemibuzo kwi nkcukacha ngezentlalo, iinkcukacha zonyango, iCAPD Regime yakho, ukutya okuthathwa ngumzimba (ngokwe 24-Hour Recall), ukutshintsa kobunzima kunye neziphumo zebiochemistry results zizofuneka.

2. Ubunzima bomzimba, ubude kunye nemiqolo yesikhumba zizofuneka.

3. Amagazi akho amathathu athathwe kuwe ngenalti azothatyathwa eklinikhiniyakho.

4. Ukusetyenziswa komgubo weproteni ukuba uceliwe ukuba uwusebenzise (isigulana kwiqela lokuqala), ngokwe ngcaciso ayalathayo ebekiweyo, ngu dietician. Inyanga enye ekhutshwayo izonikezelwa kuwe qho ngenyanga kwelandelayo indlela yovavanyo.

Abukho ubungozi obuzakubakho ekuthatheni kwakho inxaxheba kwesisifundo. Awunyanzeliswa ukuba uthathe inxaxheba kwesisifundo kwaye unalo ilungelo lokuphuma kuso akukho sigwebo. Inkqubo yezigulana zakwi cala lezintso kwisibhedlele saseFrere izoqhubeka ngokuqhelekileyo. Awuzubhatalwa ngokuthatha inxaxheba kwesisifundo,kodwa uzokufumana isidlo sasemini xa uthe wazo vavanywa.

Sizozama ukugcina zonke iinkcukacha ziyimfihlo . Iinkcukacha eziyimfihlo zingaxelwa xa sithe sacelwa ngabomthethomay be disclosed if required by law.

IiOrganization ezinokuhlola okanye zikope isifundo sakho ukuqinisekisa kwanye novavanyo lweenkcukacha inganga maqela afana na la: Ethics Committee for Medical Research and the Medicines Control Council.

Iziphumo zizokupapashwa akanya ziboniswe kwingqungquthela.

Ungahlangana no nobhala we Ethics Committee ye Faculty of Health Sciences,UFS uMs Strauss weUniversity of Free State kule nombolo (051) 4052812 ukuba unemibuzo.

Isifundo sophando,kwakunye nale nkcazelo ingentla seyichaziwe kum.Ndiyakuqonda kuthetha ntoni uzibandakanya nesisifundo kunye nokuzinikezela kwam ukuba ndibe yinxalenye.

_____	_____
Signitsha yomthathi nxaxheba	Umhla
_____	_____
Signitsha yengqina	Umhla
_____	_____
Signitsha yomguquli ntetho	Umhla

Appendix 16

Excel spread sheet: Data collection sheets (Electronic copy available too)

Appendix 1

Baseline Assessment	Subject Number	
	Group	
	Date	
	Age	
	DOB	
	Gender	
	Race	
	Distance	
	People living with pt	
	Employment	
	Aetiology	
	Morbidities	
	Medication: Name	
	Medication: Dosage	
	Medication: unit	
	Duration CAPD	
	Date CAPD started	
	CAPD solution	
	Daily exchanges	
	HD line	

Appendix 2 *(page 1 of 3)*

Baseline Assessment	Subject Number	
	Group	
	Date	
	Weight	
	Edema	
	Dry weight	
	Height	
	BMI	
	MUAC: 1	
	MUAC: 2	
	MUAC: 3	
	MUAC: ave	
	TSF: 1	
	TSF: 2	
	TSF: 3	
	TSF: ave	
	AMA	
Month 1	Subject Number	
	Group	
	Date	
	Weight	
	Edema	
	Dry weight	
	Height	
	BMI	
	MUAC: 1	
	MUAC: 2	
	MUAC: 3	
	MUAC: ave	
	TSF: 1	
	TSF: 2	
	TSF: 3	
	TSF: ave	
	AMA	

Appendix 2 *(page 2 of 3)*

Month 2	Subject Number	
	Group	
	Date	
	Weight	
	Edema	
	Dry weight	
	Height	
	BMI	
	MUAC: 1	
	MUAC: 2	
	MUAC: 3	
	MUAC: ave	
	TSF: 1	
	TSF: 2	
	TSF: 3	
	TSF: ave	
	AMA	
Month 3	Subject Number	
	Group	
	Date	
	Weight	
	Edema	
	Dry weight	
	Height	
	BMI	
	MUAC: 1	
	MUAC: 2	
	MUAC: 3	
	MUAC: ave	
	TSF: 1	
	TSF: 2	
	TSF: 3	
	TSF: ave	
	AMA	

Appendix 2 *(page 3 of 3)*

Repeat Baseline	Subject Number	
	Group	
	Date	
	Weight	
	Edema	
	Dry weight	
	Height	
	BMI	
	MUAC: 1	
	MUAC: 2	
	MUAC: 3	
	MUAC: ave	
	TSF: 1	
	TSF: 2	
	TSF: 3	
	TSF: ave	
	AMA	

Appendix 3 *(page 1 of 2)*

Baseline Assessment	Subject Number	
	Group	
	Date	
	Weight change: 2 weeks	
	Weight change: 6 months	
	Food intake: Overall	
	Food intake: Duration	
	Food intake: Type of change	
	Subcutaneous fat: Eyes	
	Subcutaneous fat: Triceps	
	Subcutaneous fat: Biceps	
	Subcutaneous fat: Chest	
	Muscle wasting: Temple	
	Muscle wasting: Clavicle	
	Muscle wasting: Scapula	
	Muscle wasting: Ribs	
	Muscle wasting: Quadriceps	
	Muscle wasting: Calf	
	Muscle wasting: Knee	
	Muscle wasting: Interosseous	
	Edema: Hand	
	Edema: Sacrum	
	Edema: Feet	
	Overall SGA Classification	

Appendix 3 *(page 2 of 2)*

Repeat Baseline	Subject Number	
	Group	
	Date	
	Weight change: 2 weeks	
	Weight change: 6 months	
	Food intake: Overall	
	Food intake: Duration	
	Food intake: Type of change	
	Subcutaneous fat: Eyes	
	Subcutaneous fat: Triceps	
	Subcutaneous fat: Biceps	
	Subcutaneous fat: Chest	
	Muscle wasting: Temple	
	Muscle wasting: Clavicle	
	Muscle wasting: Scapula	
	Muscle wasting: Ribs	
	Muscle wasting: Quadriceps	
	Muscle wasting: Calf	
	Muscle wasting: Knee	
	Muscle wasting: Interosseous	
	Edema: Hand	
	Edema: Sacrum	
	Edema: Feet	
	Overall SGA Classification	

Appendix 4 *(page 1 of 2)*

Baseline Assessment	Subject Number	
	Group	
	Date	
	Serum albumin	
	Serum sodium	
	Serum potassium	
	Serum phosphate	
	Serum urea	
	Serum creatinine	
	Serum cholesterol	
	CRP	
Month 1	Subject Number	
	Group	
	Date	
	Serum albumin	
	Serum sodium	
	Serum potassium	
	Serum phosphate	
	Serum urea	
	Serum creatinine	
	Serum cholesterol	
	CRP	
Month 2	Subject Number	
	Group	
	Date	
	Serum albumin	
	Serum sodium	
	Serum potassium	
	Serum phosphate	
	Serum urea	
	Serum creatinine	
	Serum cholesterol	
	CRP	

Appendix 4 *(page 2 of 2)*

Month 3	Subject Number	
	Group	
	Date	
	Serum albumin	
	Serum sodium	
	Serum potassium	
	Serum phosphate	
	Serum urea	
	Serum creatinine	
	Serum cholesterol	
	CRP	
Repeat Baseline	Subject Number	
	Group	
	Date	
	Serum albumin	
	Serum sodium	
	Serum potassium	
	Serum phosphate	
	Serum urea	
	Serum creatinine	
	Serum cholesterol	
	CRP	

Appendix 5

Food Record 1	Subject Number	
	Group	
	Date	
	Food Record	
	Energy	
	Carbohydrate	
	Protein- Total	
	Protein-HBV	
Food Record 2	Subject Number	
	Group	
	Date	
	Food Record	
	Energy	
	Carbohydrate	
	Protein- Total	
	Protein-HBV	
Food Record 3	Subject Number	
	Group	
	Date	
	Food Record	
	Energy	
	Carbohydrate	
	Protein- Total	
	Protein-HBV	

Appendix 6, 7, 8

Month 1	Subject Number	
	Group	
	Date	
	Days: Intake	
	Days: Missed intake	
Month 2	Subject Number	
	Group	
	Date	
	Days: Intake	
	Days: Missed intake	
Month 3	Subject Number	
	Group	
	Date	
	Days: Intake	
	Days: Missed intake	

Appendix 9

Baseline Assessment	Subject Number	
	Group	
	Date	
	Transport status	
	Weight	
	Height	
	Age	
	Urine: Urea	
	Urine: Creatinine	
	Urine: Volume	
	Dialysis: Urea	
	Dialysis: Creatinine	
	Dialysis: Volume	
	Dialysis: Albumin lost	
	Serum urea	
	Serum creatinine	
	Weekly Kt/v	

Appendix 17

Protocol Summary

Sample population and sample selection

The data will be collected at the renal unit (ward C12) of Frere Hospital in East London. This study population will consist of all patients currently on Continuous Ambulatory Pertioneal Dialysis (CAPD) at Frere Hospital. This will include ±25 patients from the ward. The whole group will be recruited for the study. All patients will be informed by the researcher about this study at the baseline nutritional assessment, and given the opportunity to partake. The percentage of patients receiving CAPD at Frere Hospital (47%) is higher than the reported South African patients receiving CAPD (32%). This highlights the importance of the small sample size at Frere Hospital, as it represents almost half of the CRF patients that are receiving Renal Replacement Therapy (RRT).

Method

The study will be a randomised controlled clinical trial. Patients will be randomised by means of median age, gender, median serum albumin and median duration on CAPD and divided into two groups according to statistical calculations. Group one (intervention group) will receive the *Protifar* powder and group two (control group/ standard care at Frere Hospital currently will not receive the *Protifar* powder.

Intervention: Protein supplementation

The participants average protein intake will be assessed at the baseline investigation of the study. Group one will be supplemented with 0.65g/kg/day protein, which is half of the 1.3g/kg/day protein requirement according to KDOQI Guidelines, in addition to their normal dietary intake.

Control method

Various control methods are set to ensure the validity and reliability. The anthropometry measurements taken by the researcher using standard practices (Appendix 2); blood collected by the same procedures currently at Frere Hospital, using defined biochemical cut-off points at the NHLS and an immediate duplicate blood sample will be taken if a result comes back as abnormally high or abnormally low (Appendix 4); MRC Food Flash Cards and Food Photo Manual will be used to establish correct portion sizes (Appendix 5); three-24 hour recalls will be used to improve validity of the results (Appendix 5); the dialysis adequacy will use both the Kt/v and creatinine clearance (using the Watson and duBois Formula) (Appendix 9); the *Speaking books* Informed Consent book will be used to obtain informed consent from illiterate patients (Appendix 10); all appendices are translated into Afrikaans and Xhosa; and all protein powder used in group one is measured out by the researcher into special containers, according to the patient's actual body weight.

Risk and adverse effects

There are no risks or adverse effects of protein powder supplementation.

Expected outcome

The patients in group one receive additional protein supplements to their normal dietary intake and thus are expected to have an improved nutritional status. The changes in nutritional status will be evaluated through the anthropometry, Subjective Global Assessment (SGA nutrition assessment tool) and biochemical measures (serum albumin). The patient's diet intake will be assessed and evaluated through the 24-Hour Recall.

Appendix 18

Dear Chief Executive Officer, Frere Hospital

RE: Permission to perform study at Frere Hospital:

The prevalence of malnutrition is significant in patients receiving CAPD and increases with hypoalbuminea. There is very little data available on CAPD in the South African setting. A need for optimal dialysis practices and dietary intervention is needed, especially in malnourished patients, to reduce their morbidity and mortality; and improve their nutritional status.

The current study aims to determine the nutritional status of the patients on CAPD at Frere Hospital, using various nutritional parameters and determining the effect of protein supplementation by means of a randomised controlled clinical trial.

This study will provide meaningful insight into the nutritional status, dialysis practices, dietary intake and dietary intervention of patients on CAPD in SA. To date no study has been done in SA to assess whether protein supplementation, by means of a protein powder, will improve the patients' overall nutritional status and serum albumin, thus decreasing the morbidity and mortality.

The patients receiving CAPD in the Renal Unit (Ward C12) at Frere Hospital will be used in the study. This will include 25 patients from the ward. The whole group will be recruited for the study. Patients will be randomised by means of age, gender, serum albumin and duration on CAPD and divided into two groups. Group one will receive the *Protifar* powder and group two will not receive the *Protifar* powder. Protifar will be supplemented at 0.65g/kg/day, which is half of the recommended protein intake, according to the kidney disease outcomes quality initiative (KDOQI).

These patients currently come into Frere Hospital on a monthly basis for their routine follow-ups, and this opportunity will be used to conduct further research as mentioned above.

The researcher intends to publish the research results in a peer-reviewed journal, and present the results at the South African Congress of Nephrology 2013 in the form of a poster presentation. Feedback to the relevant stakeholders will be given in the form of a research report and information session.

Please see the attached Protocol Summary for further information.

The research project is currently submitted for ethics approval from the Ethics Committee from the Faculty of Health Sciences, University of the Free State. Approval for the commencement of the study is also requested from Frere Hospital.

Yours Sincerely,

Brigitte Leclercq
Researcher (Masters in Human Nutrition student)
and Dietician at Frere Hospital
071 482 7437/ 043 709 2427
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9 Summary

CKD includes a variety of heterogeneous disorders which cause progressive structural or functional deterioration of the kidney (KDIGO, 2013). Renal replacement therapy (RRT), becomes necessary when accumulating waste products interfere with normal body functions, and physiologic changes can no longer be controlled by diet and medication alone (KDOQI, 2006; Schrier, 2009). Continuous ambulatory peritoneal dialysis (CAPD), uses the semi-permeable membrane of the peritoneum for dialysis, making it possible for patients to dialyse away from a dialysis unit (Wilkens, Juneja & Shanaman, 2012). No trial to date, has described the nutritional status of the CAPD population in the Eastern Cape, and the effect of protein supplementation in a South African CAPD population has not been investigated.

A randomised controlled, open-label trial, was approved by the Ethics Committee of the Faculty of Health Sciences at the University of the Free State. Of the 28 patients receiving CAPD at Frere Hospital in 2012, 26 gave informed consent and were randomised into an experimental (n=13) and a control (n=13) group according to median age, gender, median serum albumin levels and median duration on CAPD. The intervention group were supplemented with a protein powder *(Protifar)* at 0.65g/kg actual body weight. Socio-demographics, medical histories, and CAPD regiments were recorded at baseline. Nutritional status assessed in terms of anthropometry, Subjective global assessment (SGA) nutrition assessment tool and biochemistry, was followed up monthly over the four month duration of the trial. Adequacy of dialysis was also assessed. Data was analysed with SAS statistical software and compared by 95% confidence intervals for median or percentage differences.

The trial population were 76% female, 80% Black, 84% unemployed/receiving a grant; and 84% lived farther than 50 km away for Frere Hospital. Hypertension was the main cause of renal failure in 80%, and the main co-morbidity, in 92%. Most had been using CAPD for five to eight months, as four exchanges per day, and 69% also had a HD line. At baseline none were underweight based on body mass index (BMI) (calculated from dry weight); rather 35% were overweight/obese. Based on upper arm muscle area (AMA.) none were wasted. SGA nutrition assessment tool identified 23% as mildly to moderately malnourished, and only one participant as severely malnourished. Yet, most participants had inadequate intakes of energy (72%), protein (56%), HBV protein (64%), carbohydrate (52%) and fat (60%); and 92% had below normal serum albumin levels. Serum phosphate, urea and creatinine levels were elevated above normal in 44%, 96% and 100% of

participants. Based on Kt/V and creatinine clearance, 90% and 100%, respectively, were inadequately dialysed.

Protein supplementation did not statistically significantly impact on any parameter of nutritional status, although slight increases in the median dry weight, AMA and serum albumin levels, which may indicate some clinical benefit, was recorded. Compliance was generally good at above 82.% throughout the trial.

As the first trial to describe the socio-demographic and nutritional status profile of patients receiving CAPD in the EC, a similar socio-demographic profile as described in other studies for the South African CAPD population in Johannesburg, Durban and Polokwane was found (Isla *et al.,* 2014*;* Abdu *et al.,* 2011; Naicker, 2002). The anthropometric profile was however found to be very different to that described for CAPD patients in developed countries, with a high prevalence of overweight/obesity. The causes of the overall inadequate dialysis reflected in highly elevated serum levels of waste products in this study population, needs to be investigate further. Although protein supplementation did not have a statistically significant impact on the nutritional status of CAPD patients in this trial, some non-significant improvements in anthropometry and biochemical indicators, suggest that studies of larger size with supplementation over a longer period of time are needed.

10 **Opsomming**

Kroniese niersiekte sluit 'n verskeidenheid van heterogeniese versteurings in wat progressiewe strukturele of funksionele agteruitgang van die nier veroorsaak (KDIGO, 2013). Nier vervangingsterapie (NVT) raak nodig wanneer afvalstowwe inmeng met normale liggaamsfunksie, en fisiologiese veranderinge nie meer deur dieet en medikasie alleen beheer kan word nie (KDOQI 2006; Schrier, 2009). Deurlopende ambulante peritoneale dialise (DAPD) maak gebruik van die semi-deurlaatbare membraan van die peritoneum vir dialise, en maak dit moontlik vir pasiënte om weg te wees van 'n dialise-eenheid (Wilkens, Juneja & Shanaman, 2012). Tot op datum het geen studie die voedingstatus van die DAPD bevolking in die Oos-Kaap beskryf, of die effek van proteïen-aanvullings in 'n Suid-Afrikaanse DAPD bevolking ondersoek nie.

'n Gerandomiseerde gekontroleerde, nie-blinde studie is deur die Etiekkomitee van die Fakulteit Gesondheidswetenskappe aan die Universiteit van die Vrystaat goedgekeur. Van die 28 pasiënte wat DAPD by die Frere-hospitaal ontvang het in 2012, het 26 ingeligte toestemming gegee en is in 'n eksperimentele- (n = 13) en 'n kontrole (n = 13) groep volgens ouderdom, geslag, serum albumienvlakke en tydperk reeds op DAPD, gerandomiseer. Die eksperimentele groep se dieet is aangevul met 'n proteïenpoeier (*Protifar*) teen 'n dosis van 0.65g / kg werklike liggaamsmassa. Sosio-demografiese inligting, mediese geskiedenis, en DAPD regimente is by basislyn aangeteken. Voedingstatus, in terme van antropometrie, subjektiewe globale assessering (SGA) en biochemie, is maandeliks oor die vier maande verloop van die studie bepaal. Toereikendheid van dialise is ook bepaal. Data is ontleed met SAS statistiese sagteware en vergelyk met 95% vertrouensintervalle vir mediaan of persentasie verskille.

Die studie populasie was 76% vroulik, 80% Swart, 84% werkloos / op staatstoelaag; en 84% het verder as 50 km van Frere-hospitaal gewoon. Hipertensie was die hoofoorsaak van nierversaking in 80% van die deelnemers, en die vernaamste komorbiditeit in 92% van die deelnemers. Die meerderheid het al DAPD vir vyf tot agt maande gebruik, teen vier uitruile per dag, en 69% het ook 'n HD lyn gehad. Gebaseer op liggaamsmassa-indeks (LMI) (bereken met droë massa) was niemand in die studiepopuladie ondermassa by basislyn nie, en 35% was oorgewig / vetsugtig. Gebaseer op die bo-arm spierarea (BASA) was geen deelnemers ondervoed nie.

SGA het 23% as effens tot matig ondervoed geklassifiseer, en slegs een deelnemer was as erg ondervoed geklassifiseer. Die meeste deelnemers het onvoldoende inname van energie (72%), proteïen (56%), HBV proteïen (64%), koolhidrate (52%) en vet (60%) gehad; en 92% se serum albumienvlakke was laer as normaal. Serum fosfaat-, ureum- en kreatinienvlakke was hoër as normaal in 44%, 96% en 100% van die deelnemers. Gebaseer op Kt / V en kreatinienopruiming, was dialise onvoldoende in 90% en 100% onderskeidelik.

Proteïen het nie ‘n statisties beduidende invloed op enige parameters van voedingstatus gehad nie, hoewel geringe toenames in die mediaan droë gewig, BASA en serum albumienvlakke wel waargneem is, wat moontlik op 'n kliniese voordeel dui Nakoming van die supplementasie was oor die algemeen goed: bo 82% deur die verloop van die studie.

Daar is bevind dat DAPD pasiënte in die Ooskaap 'n soortgelyke sosio-demografiese profiel het as wat in Johannesburg, Durban en Polokwane, beskryf is in ander studies (Isla *et al,* 2014; Abdu *et al,* 2011; Naicker, 2002). Daar is egter bevind dat die antropometriese profiel baie verskil van wat beskryf word vir DAPD pasiënte in ontwikkelde lande, met 'n hoër voorkoms van oorgewig / vetsug. Die oorsake van die algemene onvoldoende dialise, soos weerspieël deur hoogs verhoogde serumvlakke van afvalprodukte in hierdie studie bevolking, moet verder ondersoek word. Alhoewel proteïenaanvulling nie 'n statisties beduidende impak op die voedingstatus van DAPD pasiënte in hierdie bevolking gehad het nie, dui nie-beduidende verbeterings in sommige antropometries- en biochemiese aanwysers dat aanvullingsstudies van groter omvang en langer tydsduur nodig is.

11 Ten key terms

1. **24-hour recall:** A method of dietary assessment in which an individual is asked to remember everything eaten during the previous 24 hours (Hammond, 2008).

2. **Albumin:** The most abundant (55% to 65% of total) plasma protein; a negative acute-phase respondent with a long half-life ($t_{1/2}$=21 days); maintains plasma oncotic pressure and acts as a transport protein (Levey *et al*, 2008).

3. **Arm Muscle Area:** A value obtained from the combination of the mid upper arm circumference and the tricep skin fold measurements. It is a good indication of lean body mass and thus an individual's skeletal protein reserves (Hammond, 2008).

4. **Body Mass Index:** A value that correlates with body fat and is expressed as weight in kilograms divided by height squared (BMI = kg/m^2) (Gee *et al.,* 2008).

5. **Chronic kidney disease:** Abnormalities of kidney structure or function, present for more than three months, with implications for health; and thus encompasses a variety of heterogeneous disorders which cause progressive structural or functional deterioration of the kidney and leads to different clinical presentation related to cause, severity and the rate of progression (KDIGO, 2013).

6. **Continuous ambulatory peritoneal dialysis:** Dialysis using the semi-permeable peritoneal membrane. A catheter is surgically implanted in the abdomen and into the peritoneal cavity. Dialysate containing a medium to high-dextrose concentration is instilled into the peritoneum, where diffusion carries waste products from the blood through the peritoneal membrane and into the dialysate. This fluid is then withdrawn and discarded, and new solution is added (Wilkens, Juneja & Shanaman, 2012).

7. **Dietary history:** A detailed dietary food record; may include a 24-hour recall, food frequency questionnaire, food diary, and other information such as weight history, previous diet changes, use of supplements, and food intolerances (Hammond, 2008).

8. **Hemodialysis:** The removal of certain elements from the blood by virtue of the difference in the rates of their diffusion through a semi-permeable membrane. Two distinct physical processes are involved, diffusion and ultrafiltration (Anderson *et al.,* 2008).

9. **Protein Energy Wasting:** The lack of sufficient energy or protein to meet the body's metabolic demands, as a result of either an inadequate dietary intake of protein, intake of poor quality dietary protein, increased demands due to disease, or increased nutrient losses (Wilkens, Juneja & Shanaman, 2012).

10. **Standards of care:** Practice guidelines that are established by a facility, to ensure that, at a minimum, reasonable care is rendered (Charnay *et al.,* 2008).